PERIODONTAL DISEASE AND PRETERM BIRTH IN RURAL NEPAL: A COMMUNITY-BASED PROSPECTIVE COHORT STUDY

by
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Abstract

Annually, nearly three million babies die before 28 days of life, and preterm birth is the leading cause of these deaths in high- and low-income settings. Few preventative interventions for preterm birth exist, and in low- and middle-income countries (LMICs), therapeutic interventions are often unavailable, especially in communities where many mothers deliver at home or in primary facilities without skilled care (e.g. South Asia).

There is strong observational evidence for an association between periodontal disease in pregnant women and preterm birth, but randomized controlled trials evaluating the impact of periodontal therapy on adverse pregnancy outcomes have produced inconsistent results. The mechanisms underlying this relationship are unclear; hypotheses include translocation of periodontal pathogens or their byproducts to the fetal-placental unit or action of inflammatory mediators in the periodontium on systemic inflammation. Alternatively, this observation could be the result of an unknown confounding factor, such as a genetic hyper-inflammatory phenotype.

We investigated the relationship between periodontal disease and preterm birth in a rural community in Nepal. Our aims were to: 1) review community-based studies of the periodontal disease and adverse pregnancy outcome relationship in LMICs, 2) estimate the validity of periodontal measurements collected by community-based oral health workers relative to a dentist, 3) describe the periodontal status and oral hygiene behaviors of pregnant women, and 4) assess the incidence of preterm birth among women with and without periodontal disease.

Our review found only one study of this relationship that recruited participants using a population-based sample, although several included women from multiple institutions within a community. Studies were widely heterogeneous in quality, methodology, and their results were mixed. We demonstrated acceptable agreement for measures of periodontal probing depth collected by the oral health workers and dentist. The majority of women in our population had gingivitis, but very few signs of periodontitis, and oral hygiene behaviors varied from recommended practices. Lastly, we found a slight, but statistically significant, increase in risk of preterm birth for women with periodontal disease.

We suggest the need to evaluate oral health interventions to reduce risk of preterm in low-income settings and understand the causal mechanisms behind this relationship.

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Chapter 1: Introduction

Neonatal mortality and preterm birth

Over the Millennium Development Goals (MDGs) era, substantial gains in child survival were achieved, most notably, a 53% reduction in global under-five mortality, from 91 to 43 deaths per 1,000 live births, between 1990 and 2015.[1] During the same period, neonatal mortality fell from 36 to 19 deaths per 1,000 live births.[1] Despite this progress, the global MDG 4 target of reducing under-five mortality by two-thirds, to less than 30 deaths per 1,000 live births, was not achieved.[1] Declines in mortality occurred at a faster rate for children 1-59 months than for those in their first month of life (58% vs. 47%), and the proportion of under-five deaths occurring among newborns increased by 13% from 40% to 45%.[1]

Recent research and global movements have recognized the need to increase focus on neonatal survival if further reductions in mortality among infants and children are to be achieved. In 2014, the United Nations Secretary-General launched the Every Newborn Action Plan with the goal of reducing newborn deaths to less than 10 deaths per 1,000 live births and stillbirths to less than 10 per 1,000 total births by 2035.[2,3] The Sustainable Development Goals (SDGs), adopted by the United Nations General Assembly in 2015 to build on the success of the MDGs, also included specific a focus on neonatal mortality. SDG Goal 3, *Ensure healthy lives and promote well-being for all at all ages*, aimed to reduce global under-five mortality and neonatal mortality below 25 and 12 deaths per 1,000 live births, respectively, in every country by 2030.[4]

In 2015, an estimated 2.7 million babies died before 28 days of life, accounting for almost half (45.1%) of all deaths among children under five years.[5] Almost three-quarters of these deaths occurred in the first week of life (73%) and over a third on the first day (36%).[3] The three leading causes of neonatal death globally in 2015 were preterm birth complications (35.2%), intrapartum-related events (23.5%), and sepsis/meningitis (15.0%).[51] In 2015, over a million under-five deaths were attributable to complications from preterm birth and the condition was a risk factor in 50% of neonatal deaths.[5,6] Premature babies that survive are at increased risk of mortality from other causes, especially neonatal infections, as well as long-term disability, including neurological and developmental impairments, and chronic diseases.[6]

Risk factors for preterm birth

Globally, preterm birth affected 14.9 million babies in 2010, representing 11.1% of births.[6] Preterm birth occurs in high- and low-income countries, ranging from a low of 5% in several northern European countries to a high of 18% in Malawi.[7] The highest rates of preterm birth are observed in low- and middle-income income (LMICs) countries, predominantly in Sub-Saharan Africa and South Asia, although high rates are also found in some high-income countries, such as the United States (12.0%).[7] More than 60% of all preterm births occur in Sub-Saharan Africa and South Asia, which together are responsible for half (52%) of global live births.[7] In countries with high rates of preterm birth, the condition is more likely to be spontaneous than provider-initiated, due to the limited availability of services for caesarean birth, which occur in less than 5% of births

[1] Other causes of neonatal death in 2015 were congenital abnormalities (11.4%), pneumonia (6.0%), tetanus (1.3%), and diarrhea (0.7%).

in some African countries.[7] Although data on preterm births are not routinely collected in many countries, for those with reliable data, preterm birth rates have generally increased in recent years.[6]

Preterm birth is defined as gestation less than 37 weeks[2], and is further subdivided into moderate preterm (32 to <37 weeks), very preterm (28 to <32 weeks), and extremely preterm (<28 weeks). Gestation lasting ≥42 weeks is considered postterm. Preterm births are classified as either spontaneous (including onset of preterm labor or premature rupture of membranes) or provider-initiated (including induction of labor or caesarean birth) due to maternal or fetal indications.

Spontaneous preterm birth is a multi-factorial condition that has a variety of genetic, life style, and environmental risk factors. The etiologies of preterm birth differ based upon gestational age; for example, intrauterine infection is estimated to cause 50% of extremely preterm births (<28 weeks), while beyond 34 weeks, premature births caused by intrauterine infection are rare.[8] Males are at slightly higher risk of preterm birth (55% of preterm births are boys), stillbirth, and neonatal mortality, compared to girls at the same point in gestation.[9,10] Risk factors for preterm birth include young or advanced maternal age; multiple births; pregnancy history, especially previous preterm birth and short pregnancy intervals; infections, including urinary tract infections, bacterial vaginosis, sexually transmitted infections (e.g. syphilis), HIV, and malaria; life style factors such as smoking, alcohol use, drug use, and stress and excessive physical

[2] Measured from the first day of the last menstrual period.

exertion; ethnicity and genetics; and chronic conditions or diseases, including anemia, undernutrition, high body mass index (BMI), hypertension, and diabetes.[6,8]

Prevention & treatment for preterm birth

The majority of preterm births occur after 32 weeks gestation (84%), a point where survival is likely when appropriate care is available.[7] Actual survival of preterm babies, however, varies drastically between high- and low-income countries: almost all babies born at 32 weeks will survive in high-income countries compared to only 50% in low-income countries.[7] In LMICs, where most preterm babies are born, preventative and therapeutic interventions are often unavailable, and have proven difficult to scale up, especially in communities where many mothers deliver at home or in primary facilities without skilled care, as is common in South Asia.[11] Interventions to reduce newborn death and preterm birth target women across the continuum of care, including preconception, antenatal, intrapartum, and postpartum periods.[12]

A 2010 review by the Global Alliance for Prevention of Prematurity and Stillbirth (GAPPS) identified 11 evidence-based ***treatment/therapeutic*** interventions for improving survival of preterm infants, including prophylactic steroids for preterm labor, antibiotics for preterm labor with premature rupture of membranes, vitamin K supplementation at delivery, case management of neonatal sepsis and pneumonia, delayed cord clamping, room air (vs. 100% oxygen) for resuscitation, hospital-based kangaroo mother care, early breastfeeding, thermal care immediately after birth, surfactant therapy, and application of continued distending pressure for respiratory distress syndrome.[11] In 2015, the World

Health Organization (WHO) released guidelines for interventions to improve preterm birth outcomes, strongly recommending antenatal corticosteroids for women at risk of preterm birth from 24 to 34 weeks gestation, magnesium sulfate for women at risk of preterm birth <32 weeks to protect again fetal neurological complications, antibiotics for preterm prelabor rupture of membranes, kangaroo thermal care for newborns <2,000 g at birth, continuous positive airway pressure for newborns with respiratory distress syndrome (RDS), surfactant replacement therapy for newborns with RDS in facilities properly equipped and staffed, and oxygen therapy at 30% or air rather than 100% oxygen during ventilation of newborns <32 weeks.[13] While some of these treatment/therapeutic management interventions can be implemented at high coverage even in low resource settings, the need for interventions that can prevent preterm birth is critical. The evidence base for preventative interventions, however, is weak; the GAPPS review identified only two ***preventative*** interventions for preterm birth with strong evidence: smoking cessation and progesterone therapy to prevent reoccurrence of preterm birth among women at high risk.[11]

Periodontal disease and preterm birth

Periodontal disease includes a group of inflammatory conditions, typically initiated by oral bacteria, progressing from reversible accumulation of plaque and inflammation of gingival tissue (gingivitis) to irreversible breakdown of the supportive tissues of the teeth and eventually tooth loss (periodontitis).[14] Periodontal disease is one of two major oral diseases, along with dental caries, and affects populations in every region of the world.[15] Globally, gingivitis is highly prevalent, and severe periodontitis affects 10% to 15% of adult populations.[16] Gingivitis often worsens in extent and severity in women during pregnancy, peaking in the second or third trimester.[17,18] Smoking and diabetes are two important risk factors for periodontitis, affecting both initiation and progression of the disease.[14,19,20] Other risk factors for periodontal disease include older age, poor oral hygiene, alcohol consumption, stress, malnutrition, and other chronic diseases.[15] There is substantial variation in prevalence of periodontal disease within countries, and associations have been observed with distal factors such as income and education, urban/rural location, race, and ethnicity.[21]

Proper oral hygiene can generally prevent gingivitis and severe periodontitis.[14] Tobacco cessation is also a critical component of periodontal disease prevention.[14] Treatment for periodontal disease can include scaling and root planing, surgery (in some cases), management of systemic diseases, tobacco cessation, and improved oral hygiene.[14] In many LMICs, oral health facilities, equipment, and personnel, are in short supply, severely limiting access to oral health care, especially preventative services.[22]

Studies have found associations between periodontal disease and several systemic conditions, including diabetes mellitus, cardiovascular diseases, and adverse pregnancy outcomes.[23,24] There is strong observational evidence for an association between periodontal disease in pregnant women and preterm birth,[23,25] but randomized controlled trials (RCTs) evaluating the impact of periodontal therapy during pregnancy on adverse pregnancy outcomes have produced inconsistent results.[26] The mechanisms underlying the observed relationship are unclear, but hypotheses include hematogenic translocation of periodontal pathogens or their byproducts to the fetal-placental unit or the action of inflammatory mediators in the periodontium on levels of systemic inflammation.[27] Alternatively, the association could be driven by a common confounding factor, such as a genetic hyper-inflammatory phenotype, responsible for both the increased risk for periodontal disease and adverse pregnancy outcomes.[28]

A meta-analysis of eleven prospective cohort studies by Chambrone et al. (2011) found a significant association between periodontitis and preterm (Relative risk (RR) 1.70, 95% CI: 1.03, 2.81), low birth weight (RR 2.11, 95% CI: 1.05, 4.23), and preterm term low birth weight (RR 3.57, 95% CI: 1.87, 6.84).[29] Other systematic reviews and meta-analyses of observational studies have generally supported the existence of a positive, independent association between periodontal disease and adverse pregnancy outcomes.[25,29-34] However, reviews have noted that studies of this association vary widely in study design, methodology, and quality; method and timing of periodontal assessment; definition of periodontal disease; method of gestational age assessment; control of important confounders; and the prevalence and severity of periodontal disease, adverse pregnancy outcomes, and confounding factors in study populations. A study by Manau et al. (2008) demonstrated that both the prevalence of periodontitis in the sample of pregnant women and the significance of the association between periodontal disease and adverse pregnancy outcomes can vary with the choice of definition or measurements for periodontal disease.[353]

[3] Manau et al (2008) applied 14 definitions of periodontitis, which had previously been used in studies of this association, to their study population, finding that, for most definitions, periodontal disease was higher in the adverse pregnancy outcome group, but was only statistically significant in a few cases, typically when the assessment was based upon assessment of clinical attachment loss (CAL).

A meta-analysis of thirteen randomized trials of oral health interventions by Chambrone et al. (2011) found that although roughly half (n=8) of the included studies reported reductions in adverse pregnancy outcomes, pooled results showed no decrease in risk of preterm birth (RR 0.88, 95% CI: 0.72, 1.09), low birth weight (RR 0.78, 95% CI: 0.53, 1.17), or preterm low birth weight (RR 0.52, 95% CI: 0.08, 3.31).[36] Authors of several meta-analyses of interventional studies cited similar issues to those in the observational literature regarding heterogeneity in populations, methodology, and quality among studies. Some meta-analyses reported finding sub-groups of studies for which periodontal therapy reduced risk for adverse pregnancy outcomes, including studies with populations at high risk of preterm birth,[37] high quality studies with demonstrated control of periodontal disease,[38] studies with participants with less severe periodontal disease,[39] or studies utilizing a cointervention of chlorhexidine oral rinse[26] Several other meta-analyses, however, concluded no effect of periodontal therapy on adverse pregnancy outcomes, including two that found that the subgroup of studies with unclear or high risk of bias showed reduced risk of preterm birth while studies with low risk of bias did not.[36,40-42]

Nepal

Neonatal health in Nepal

Nepal is a landlocked country in South Asia with a population of 28.5 million (2015).[43] Geographically, Nepal is divided into three regions, the mountain region in the north, hill region along the middle of the country, and the plains, or Terai, in the south. Nepal spent the equivalent of 5.8% of its 19.8 billion gross domestic product (GDP) on health in

2014.[44] Per capita total spending on health spending in Nepal was $137 (PPP int$), 40.3% in the form of government expenditure and 59.7% private expenditure, the majority of which was out-of-pocket (79.9%).[44] Government spending on health care was only 11.3% of total government spending in Nepal in 2014.[44]

Nepal met its Millennium Development Goal (MDG) 4 target to reduce under five mortality by two-thirds, to 54 deaths per 1,000 live births, achieving a reduction of 141 to 36 deaths per 1,000 live births between 1900 and 2015.[14] During that period, the neonatal mortality rate dropped from 59 to 22 deaths per 1,000 live births.[1] Nepal's 2016 Demographic and Health Survey (DHS) reported an under-five mortality rate of 39 deaths per 1,000 live births and neonatal mortality of 21 deaths per 1,000 live births.[45] Leading causes of neonatal death, as reported by Nepal's 2006 DHS, were acute respiratory infections, diarrhea, and other infections (39%); birth asphyxia and birth injury (33%); congenital anomalies (8%); preterm birth and low birth weight (6%); and other causes (13%).[46] Given reductions in neonatal mortality rate between 2006 and 2016 DHS estimates, the current cause distribution likely includes a substantially higher proportion of deaths arising from complications of preterm birth. In 2010, Nepal had an estimated 723,500 live births and rate of preterm birth of 14.0%.[7]

Recently, Nepal's Ministry of Health and Population (MoHP) has undertaken several major initiatives that have contributed to reductions in under-five and neonatal mortality. Nepal's National Health Policy 2014 called for universal coverage of basic health services, operationalized through the four "strategic directions" of the Nepal Health

[4] Nepal achieved an annual rate of reduction in under-five mortality of 5.5% between 1990 and 2015.

Sector Strategy (NHSS 2015-2020): equitable access to health services, quality health services, health systems reform, and multi-sectoral approach.[47] In 2016, Nepal launched the Nepal Every Newborn Action Plan with the goal of reducing newborn deaths to below 11 deaths per 1,000 live births and stillbirths below 13 per 1,000 births by 2035.[48] Guided by the frameworks provided by these and other national policies, Nepal has worked to strengthen the delivery of maternal and child health inventions through a series of national programs such as the National Safe Motherhood Program (2012-2017) and Community-Based Newborn Care Package.[48]

Oral health in Nepal

The oral health status of pregnant women in low-resource communities such as Nepal has not been well characterized, and few studies have assessed the oral health and hygiene practices of adult Nepalis.[49] Nepal's only official national survey for oral health, the *Nepal National Oral Health Pathfinder Survey*, was conducted by Yee et al. in 2004.[50-53] In the 15-16 year age group, Community Periodontal Index (CPI) scores were 26% periodontal health (CPI 0), 8% bleeding on probing (BOP) (CPI 1), 61% BOP and calculus (CPI 2), 5% probing depth 4-5 mm (CPI 3), and 0% PD ≥6 mm (CPI 4).[50] Among 35-44 year-olds, CPI scores were 7% periodontal health (CPI 0), 3% BOP (CPI 1), 27% BOP and calculus (CPI 2), 48% PD 4-5 mm (CPI 3), and 16% PD ≥6 mm (CPI 4).[50] The mean number of sextants with calculus (or higher CPI score) was 2.0 for the 15-16 year age group and 4.1 for the 35-44 age group.[50] Living in a rural location was associated with higher CPI scores in both age groups.[51,52]

Nepal's MoHP released the *National Oral Health Strategy* and *National Strategic Plan for Oral Health* in 2004, with the goal of providing Nepalis equitable access to preventive, curative, and rehabilitative oral health care.[54] Despite this effort, most Nepalis are without access to appropriate oral health care and human resources for oral health in Nepal are inadequate.[55-57] An accurate count of the number of dentists and dental hygienists in the country has not been maintained by Nepal's government; [58] however, a 2008 estimate put the number of dentists in Nepal at 624, the equivalent of only 2 per 100,000 population, one of the lowest ratios among South Asian countries.[59,60] The number of dental hygienists in 2008 was estimated to be 234.[61] A worldwide survey of human resources for oral health (2000) found only 14% of dentists in Nepal were employed by government services, while 78% were employed by private practices, 4% universities, and 4% other places.[62] Dental health professionals have reported concern about finding employment due to the limited number of government jobs and increasing number of oral health training programs.[58]

Oral hygiene behaviors in Nepal

Proper oral hygiene is critical for prevention of periodontal disease.[14] However, little is known about the oral hygiene behaviors of adults across cultural groups or regions of Nepal. A national cross-sectional survey conducted by Thapa et al. (2016) found that 95% of adult Nepalis brushed their teeth once per day, and 10% twice per day, a finding supported by two other studies.[55,63,64] Those brushing their teeth twice per day were more likely to be female and have a higher level of education.[55] Nepalis typically brushed their teeth in the morning, as part of the bathing routine.[63] Most (88%) used a toothbrush,[55,63,65] and one study reported that 89% cleaned their tongue, and 7% used interdental cleaning methods.[64] Brushes were replaced by participants either between 1-3 months (42%), 3-6 months (33%), or when worn out (25%).[63] Datiwan, a local teeth cleaning instrument fashioned from the twigs of a variety trees, was used by 3% to 18% of participants in three different studies.[63-65] Studies reported a range of 50% to 71% of participants used fluoridated toothpaste;[55,63,65] in one study, individuals who used fluoride were more likely to be younger, higher educated, and living in the Hill or Mountain regions, as compared to the Terai region.[55]

Thapa et al. (2016) collected information on oral health care seeking; very few surveyed (4%) had visited a dentist in the last 6 months, those that had tended to be older, living in an urban location, female, and higher educated.[55] Roughly one-third (32%) had ever experienced some type of dental health problem, specifically, tooth pain (71%), bleeding gums (12%), swollen gums (9%), bad mouth breathing (3%) and other (5%). Care sought by these individuals was varied, with the majority not seeking any care (52%), and the remainder visiting a medical practitioner (20%), dentist (17%), pharmacist (8%), or friends (3%).[63] A study by Knevel et al. (2010) reported that 32% of rural woman experiencing oral pain would visit a dentist, 25% a physician, and the remainder either a medicine shop, traditional medicine provider, or other health professional.[65]

Buunk-Wekhoven et al. (2011) conducted a study to identify predictors of oral hygiene behavior in Nepal.[64] Using the Oral Hygiene Behavior (OHB) index, and guided by the Theory of Planned Behavior – which incorporates attitudes, social norms, and control, as determinants of health behavior – the authors concluded that Nepalis' attitudes and perceived social norms towards oral health were not related to their oral hygiene behaviors.[64] Instead, the most important predictor of oral hygiene behaviors was perceived control over the oral hygiene behaviors.[64] Their recommendation for future interventions to improve oral hygiene in Nepal was to focus on increasing perceived control, for example, through instruction and feedback on how to execute appropriate behaviors.[64] Focusing on changing attitudes towards oral health, however, would be unlikely to succeed because Nepalis already view oral hygiene behavior positively and attach high value to the positive social outcomes of having healthy teeth, and these factors were unrelated to their oral hygiene behaviors. [64]

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Chapter 2: Review of community-based studies of the oral health and adverse pregnancy outcome association in low- and middle-income countries

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Background

Annually, almost three million babies die prior to 28 days of life, and adverse pregnancy outcomes, particularly preterm birth, are the leading cause of these deaths in both high- and low-income settings.[1] Few interventions have demonstrated efficacy to reduce risk of preterm birth, and little progress has been made in preventing preterm birth in any setting.[2] In low- and middle-income countries (LMIC), where the majority of preterm babies are born, therapeutic interventions are often unavailable and difficult to scale up, especially in communities where many mothers deliver at home or in primary facilities without skilled care (e.g. in South Asia).

Periodontal disease includes a group of inflammatory conditions, commonly initiated by oral bacteria, progressing from reversible inflammation of the gingiva (gingivitis) to irreversible breakdown of the supporting tissues of the teeth (periodontitis). Nearly 50% of U.S. adults are affected by periodontitis, with associated alveolar bone loss.[3] The World Health Organization estimates that 10% to 15% of the world populations suffer from severe periodontitis.[4] In pregnancy, normal gestational elevations in sex steroids are commonly associated with exacerbations in the severity of gingival inflammation, affecting 40% or more of women.[5]

Periodontal disease has been associated with adverse pregnancy outcomes, but the potential mechanisms underlying the observed association are unclear.[6] Proposed hypotheses include direct hematogenic translocation of periodontal pathogens or their byproducts to the fetal-placental unit or the action of inflammatory mediators from the periodontium on levels of systemic inflammation.[7,8] Alternately, the observed relationship could arise from a common factor, such as a genetic hyper-inflammatory phenotype, responsible for both increased risk for periodontal disease and adverse pregnancy outcomes.

There is strong observational evidence for an association between periodontal disease and adverse pregnancy outcomes; however, randomized controlled trials (RCTs) have failed to consistently find that periodontal treatment during pregnancy reduces risk for adverse pregnancy outcomes.[9] Subgroup comparisons suggest that the benefit of periodontal treatment may be limited to pregnant women with periodontitis at high risk for preterm birth.[10] Studies have been conducted in both high- and low-income countries and populations with varying risk for periodontal disease and adverse pregnancy outcomes. The majority of studies have been based in an academic hospital-based setting. In LMICs, participants seeking care at health facilities often differ substantially from those not seeking care, potentially biasing the measure of association, if the risk for the exposure and outcome are dissimilar in these two populations. Community-based studies aim to enroll a representative sample of the population to estimate the association of interest without selection bias. We reviewed observational and interventional community-based studies of the periodontal disease and adverse pregnancy outcome association conducted in LMICs.

Methods

We systematically searched the MEDLINE database for relevant articles published through November 24, 2016, without language or publication date restrictions. Terms were categorized into two concepts, periodontal disease and adverse pregnancy outcomes, and included the following:

("Periodontal" OR "Periodontitis" OR "Gingival" OR "Gingivitis") AND ("Preterm" OR "Premature" OR "Prematurity" OR "Early spontaneous" OR "Early birth" OR "Early labor" OR "Birth weight" OR "Birthweight" OR "Small for gestational age" OR "Intrauterine growth restriction" OR "Pre-eclampsia" OR "Preeclampsia" OR "Stillbirth" OR "Miscarriage" OR "Pregnancy outcomes").

Publications identified from the search were screened by a single reviewer (DJE). The review process followed two steps: title and abstract review and full-text review. Articles meeting all of the eligibility criteria after this process were included in our study. We included community-based randomized trials, non-randomized trials, cohort studies, case-control studies, and cross-sectional studies reporting original data on the periodontal status of pregnant women and associations with adverse pregnancy outcomes in LMICs.

Studies conducted in high-income countries (HIC) or utilizing other research designs, including case reports, reviews and opinion pieces, and animal studies, were not included. Community-based studies were defined as studies recruiting patients: 1) in a home setting using a population-based sample, 2) in two or more hospitals or antenatal clinics, or 3) in a single institution responsible for a portion of the population's deliveries that was sufficiently large to presume broad representativeness. Studies recruiting participants from only one institution that did not meet the third criteria above, for example, a specialty teaching hospital whose clients could not reasonably be presumed to represent the broader population, were excluded. Primary exposures included gingivitis and periodontitis, assessed through clinical examination. Primary outcomes included preterm birth, low birth weight, composite outcomes such as preterm low birth weight, preeclampsia, stillbirth, and miscarriage. Periodontal therapy (root scaling and planing) was the only intervention reviewed, although studies may have included cointerventions, such as oral hygiene instruction.

Data were abstracted into a table and analyzed by two reviewers. We abstracted data on measures of association for periodontal disease and adverse pregnancy outcomes from the text or tables, and when necessary and possible, calculated relative risks or odds ratios and constructed confidence intervals. Our abstraction also included data on study population, sample size, inclusion and exclusion criteria, participant age, exposure and outcome definitions, and confounders considered in the analysis.

Results

A total of 953 articles were identified by the database search. Screening of title and abstract excluded 825 articles, and full-text review eliminated another 104 articles. One interventional trial conducted in Brazil met the community-based criteria for inclusion, but did not report data on the association between periodontal disease and an adverse pregnancy outcome in the control group (independent of the intervention and control group analysis) and hence was excluded from this review.[11,12] The remaining 24 articles were classified into three tiers for analysis: 1) prospective cohort studies (n=1) in a home setting with a population sample, 2) prospective cohort studies in a hospital or clinic setting (n=6), and 3) case-control and cross-sectional studies in a hospital or clinic setting (n=17) (Table 1).

Tier 1: Prospective cohort studies in a home setting with a population sample

Only one study met the strictest inclusion criteria as a Tier 1 community-based study of the periodontal disease and adverse pregnancy outcome association. Mobeen et al. (2008) reported on a prospective, community-based cohort study of 1,152 women in a periurban area of Latifabad in Hyderabad District, Pakistan.[13] Women 20-26 weeks gestation were enrolled during routine home visits by the "Lady Health Workers" of the Pakistan Ministry of Health. Questionnaires, ultrasound and physical examinations, and oral health assessments were subsequently conducted at a local research clinic, and birth outcomes were ascertained through a second home visit or at the local health facility where the birth occurred. Moderate periodontal disease was common in this population, according to four measures: probing depth (PD), clinical attachment loss (CAL), gingival index (GI), and plaque index (PI), and their corresponding definitions (e.g. 76% had ≥3 teeth with PD ≥3 mm). Risk for stillbirth increased across quartiles of all four measures of periodontal disease, and trends for PI (aRR 1.29, 95% CI: 1.01, 1.63)[1] and GI (aRR 1.33, 95% CI: 1.03, 1.72) were significant, comparing the highest and lowest disease quartiles.[2] Risk for neonatal death increased significantly, with a dose-response relationship, across quartiles of three of four periodontal disease measures, including PD (aRR 1.42, 95% CI: 1.08, 1.87), CAL (aRR 1.36, 95% CI: 1.05, 1.77), and GI (aRR 1.38, 95% CI: 1.07, 1.78), comparing the highest and lowest quartiles. Risk of early preterm birth (<32 weeks) increased across periodontal disease quartiles for the four measures, but these trends were not significant; late preterm (<37 weeks) and low birth weight were not significantly different across quartiles of periodontal disease.

Tier 2: Prospective cohort studies in a hospital or clinic setting

A non-randomized trial by Cruz et al. (2010) conducted across twelve public health clinics in Feira de Santana, Brazil, met the criteria for Tier 2.[11] In addition to evaluating their intervention, the study estimated the risk of low birth weight between two groups of controls: control group 1 (n=145) included women without periodontitis monitored every four weeks to maintain periodontal health during pregnancy, and control group 2 (n=53) included women with periodontitis (≥4 teeth with ≥1 site with PD ≥4 mm, CAL ≥3 mm, & BOP at the same site) who declined participation or did not show up to receive the intervention.[11] In the final adjusted model, the risk of low birth weight was found to be

[1] Adjusted relative risk and corresponding 95% confidence interval (aRR, 95% CI).
[2] Relative risks were adjusted for maternal age, education, and employment status.

twice as high among those with periodontitis, although of borderline significance (aRR 2.04, 95% CI: 0.98, 3.58).[11]

Five prospective cohort studies based in a hospital or clinic setting, including four from Asia and one from Africa, also qualified for Tier 2. Alchalabi et al. (2013) collected data on 277 pregnant women ≤20 weeks randomly selected from multiple antenatal care centers in northern and southern regions of Jordan.[14] Periodontitis (≥4 teeth with ≥1 site with PD ≥4 mm & CAL ≥3 mm) was identified in 31% of women and associated with preterm birth (aOR 4.4, 95% CI: 1.7, 11.7)[3], low birth weight (aOR 3.5, 95% CI: 1.6, 7.5), and preeclampsia (aOR 2.7, 95% CI: 1.2, 6.0). A study conducted in Malaysia, by Saddki et al. (2008), enrolled 500 women in two clinics randomly selected from a possible ten clinics in Kota Bharu District. Of the women screened for inclusion, 41% had periodontal disease (≥4 sites with ≥4 mm & CAL ≥3 mm), and this exposure was positively associated with low birth weight (aOR 3.84, 95% CI: 1.34, 11.05).[15] Ali et al. (2012) reported on a diverse population of 73 Malay, Chinese, and Indian women 28-36 weeks recruited from two hospital-based antenatal clinics and three community-based antenatal clinics in Malaysia.[16] Half (51%) of women had periodontal disease (≥2 teeth with ≥5 mm PD & CAL ≥3 mm), and no association was found with preterm birth (RR 0.39, 95% CI: 0.13, 1.13)[4] or low birth weight (RR 1.46, 95% CI: 0.26, 8.23). Sharma et al. (2007) included 670 women, from both urban and rural communities, at two hospital antenatal clinics in Fiji.[17] The authors defined periodontal disease according to the Community Periodontal Index (CPI) and reported a significant association (RR 7.06, 95% CI: 2.4,

[3] Adjusted odds ratio and corresponding 95% confidence interval (aOR, 95% CI).
[4] Unadjusted relative risk and corresponding 95% confidence interval (RR, 95% CI).

20.6) between moderate to severe periodontitis and preterm birth.[18] Rakoto-Alson et al. (2010) recruited 204 women 20-34 weeks from three public antenatal clinics in Madagascar.[19] Seventy-seven percent of participants had signs of gingivitis, and 23% had periodontitis. Slight periodontitis (≥3 sites with CAL ≥4 mm but not 3 sites with CAL ≥6 mm), relative to gingivitis (BOP with <3 sites with CAL ≥4 mm), was associated with preterm birth (RR 10.9, 95% CI: 5.4, 22.1), low birth weight (RR 13.1, 95% CI: 4.9, 35.0), and preterm low birth weight (RR 41.9, 95% CI: 9.2, 191.7).

Tier 3: Case-control and cross-sectional studies in a hospital or clinic setting

Of seventeen case-control or cross-sectional studies of the periodontal disease and adverse pregnancy outcome association, half were conducted in Brazil (n=8), and the others in six other countries: India (n=2), Iran (n=2), Thailand (n=2), Uganda (n=1), and Vietnam (n=1), China (n=1). Outcomes considered included preterm birth, low birth weight, preterm low birth weight, and pre-eclampsia. Most studies assessed the periodontal health of participants within 24 to 72 hours after delivery.

Three case-control studies evaluated preterm birth (case: <37 weeks gestation; control: ≥37 weeks gestation) as the primary outcome. A study of 300 low-income women (41% urban, 59% rural) in two hospitals in Kerala identified periodontitis (≥4 teeth with ≥1 sites with PD ≥4 mm & CAL ≥3 mm at the same site) in 18% of participants, finding a significant association with preterm birth (aOR 2.72, 95% CI: 1.68, 6.84).[20] A study of 390 women (cases: 37% urban, 63% rural; controls: 48% urban, 52% rural) in Vietnam also found a significant relationship between periodontitis (≥4 teeth with ≥1 site with PD

≥4 mm, CAL ≥3 mm, or BOP) and preterm birth (aOR 4.47, 95% CI: 2.43, 8.20).[21] A large study of 934 women at multiple hospitals in Bangkok, Thailand diagnosed either mild, moderate, or severe periodontitis (≥1 teeth with interproximal sites with PD ≥4 mm & CAL & ≥4 mm (mild), or CAL ≥5 mm (moderate), or CAL ≥6 mm (severe)) in 74% of participants.[22] However, this study found no difference in prevalence of periodontal disease between preterm birth cases and controls for any severity periodontitis (mild: aOR 1.01, 95% CI: 0.73, 1.41; moderate: aOR 1.20, 95% CI: 0.79, 1.84; severe: aOR 1.20, 95% CI: 0.67, 2.16).

Four studies evaluated low birth weight (case: <2,500 g birth weight; control: ≥2,500 g birth weight) as a primary outcome, including two large studies in Brazil. One study enrolled 584 women (cases: 71% urban, 29% rural; controls 74% urban, 26% rural) from two public hospitals in Brazil, finding a prevalence of periodontitis (≥4 teeth with ≥1 sites with PD ≥4 mm & CAL ≥3 mm & BOP at the same site) of 43% and 30% in cases and controls, respectively.[23] The study identified a significant association between periodontitis and low birth weight only among those with a lower level of education (low education (≤4 years): aOR 2.3, 95% CI: 1.14, 4.61); high education (>4 years): aOR 1.38, 95% CI: 0.84, 2.26).[23] Another study of 951 Brazilian women at three public institutions reported a prevalence of periodontitis (≥4 teeth with PD ≥4 mm & CAL ≥3 mm & BOP at the same site) of 16% and 17% for cases and controls and no association with low birth weight (aOR 1.00 95% CI: 0.57, 1.69).[24] Dasanayake et al. (1998) assessed the periodontal health of 55 pairs of Thai women, matched on age, marital status, race, gravidity, and parity, and found that women with a higher number of healthy sextants, assessed using the Community Periodontal Index of Treatment Needs (CPITN),[5] were less likely to have had a low birth weight baby (OR 0.3, 95% CI: 0.12, 0.72).[25] A study of 88 women in Iran by Haerian-Ardakani et al. (2013) also used the CPITN, reporting that the proportion of sextants with a periodontal pocket of ≥4 mm was 1.6 times (precision estimate not reported) higher in women with low birth weight babies.[26]

Four studies in this tier examined pregnancy hypertension or preeclampsia as a primary outcome, typically defined as BP ≥140/90 mmHg and proteinuria after 20 weeks gestation. A study by Politano et al. (2011) followed 116 women at two referral hospitals in Brazil, finding a positive association (aOR 3.37, 95% CI 1.32, 10.58) between periodontitis (≥2 sites with PD ≥4 mm & CAL ≥4 mm & BOP) and preeclampsia.[27] Pralhad et al. (2013) studied 200 women at three maternity hospitals in India, reporting a significant relationship (OR 5.5, 95% CI: 2.7, 11.4) between periodontal disease (oral hygiene index >3, GI >1, PD >4 mm, or CAL >3 mm) and pregnancy hypertension (BP ≥140/90 mmHG after 20 weeks gestation with or without proteinuria).[28] A third study, conducted by Sayar et al. (2011), also found a significant association between periodontitis (CAL ≥3 mm) and preeclampsia (aOR of 4.1, 95% CI: 1.5, 11.5) among 210 women in multiple hospitals in Iran.[29] Lohsoonthorn et al. (2009) included 300 women in three hospitals in Thailand and reported no association between any severity of periodontal disease (severe periodontitis: ≥2 nonadjacent teeth with interproximal sites with PD ≥4 mm & CAL ≥6 mm) and preeclampsia (severe PD: aOR 0.92, 95% CI: 0.26, 3.28).[30]

[5] Briefly, the Community Periodontal Index of Treatment Needs (CPITN) is defined as the following: 0 – health, 1 – bleeding, 2 – calculus, 3 – pocket of 4-5 mm, 4 – pocket of ≥6 mm.

Six studies, in Brazil (n=4), Uganda (n=1), and China (n=1) considered multiple outcomes or a composite outcome, preterm low birth weight, defined as gestational age at birth <37 weeks and birth weight <2,500 g. Three of the Brazilian studies reported no associations between periodontal disease and the adverse pregnancy outcomes considered. Lunardelli et al. (2005) enrolled a cross-section of 449 primarily urban women from a single institution in a Brazilian community where the majority (>99%) of births occur, finding no relationship between periodontal disease (≥1 site with PD ≥3.5 mm) and preterm birth (aOR 2.2, 95% CI: 0.8, 6.3) or low birth weight (aOR 2.0, 95% CI: 0.8, 4.8).[31] Bassani et al. (2007) followed 915 women, and found no association between periodontitis (≥3 sites in different teeth with ≥3 mm CAL) and low birth weight (aOR 0.93, 95% CI: 0.63, 1.41) or preterm low birth weight (aOR 0.92, 95% CI: 0.54, 1.57).[32] Vettore et al. (2008) found periodontitis to be more prevalent in the control participants for low birth weight and preterm low birth weight outcome groups in a study at four public maternity referral hospitals for high-risk pregnancies.[33] Alves et al. (2006), however, examined 59 women using a modified periodontal screening and recording criteria definition and reported a positive, significant association with preterm low birth weight (OR 8.9, 95% CI: 2.2, 35.7)[6].[34] Muwazi et al. (2014) found no association between periodontal disease (CPI) and preterm birth or low birth weight among 400 women in Uganda; however gingival recession was positively associated with normal birth weight (RR 1.4, 95% CI: 1.1, 1.8).[35] A study by Kang et al. (2009) in four hospitals in Beijing (two in urban and two in suburban areas) reported significant relationships between percent of sites with PD ≥4 mm (p<0.01), CAL ≥2 mm (p<0.01), and BOP

[6] Odds ratio and corresponding 95% confidence interval (OR, 95% CI).

(p<0.01) and preterm low birth weight.[36] It should be noted that the exposure measurement in this study was conducted within 1 to 2 years after delivery.[36]

Discussion

Our review identified only one study of the periodontal disease and adverse pregnancy outcome relationship that recruited participants in a home setting using a population-based sample in an LMIC. This study by Mobeen et al. (2008) of urban Pakistani women found significant associations of varying degrees between measures of periodontal disease and neonatal deaths, perinatal deaths, and stillbirth. Risk for early preterm birth (<32 weeks) increased with severity of periodontal disease (aRRs ranging from 1.65 to 2.26), but only a small number of babies in this category (n=27) were available, leading to instability in the estimated association. Among the studies recruiting participants from two or more hospitals or clinics, five of the six studies reported a significant association between periodontal disease and at least one adverse pregnancy outcome. Among case-control studies, conflicting results were found within each group of adverse pregnancy outcomes considered.

Some studies reported measures of association of a magnitude that could be considered to have public health significance, but were not statistically significant, a potential result of small sample sizes or low outcome prevalences. Cruz et al. (2010) found twice the risk of low birth weight in women with periodontitis compared to those with periodontal health, but this investigation was not the primary aim of the trial and there was insufficient power to detect an association of this magnitude.[11] Even after adjusting for a range of potential confounders, Lunardelli et al. (2005), for example, estimated the odds of preterm birth and low birth weight was more than twice as high among women with periodontal disease, but the small sample size resulted in wide confidence intervals. Previous systematic reviews of observational studies have generally supported the existence of a positive, independent association between periodontal disease and adverse pregnancy outcomes. Despite this conclusion, those reviews, like ours, noted wide variations in study design, methodology, and quality; method and timing of periodontal assessment; definition of periodontal disease; method of gestational age assessment; control of important confounders; and the prevalence and severity of periodontal disease, adverse pregnancy outcomes, and confounding factors in the study populations.[37-43] In an effort to examine this association in a wide variety of populations, we made no restrictions based on study quality or methodological characteristics. As a result, several studies included in this review, including two cohort studies, failed to control appropriately for confounders,[16,17 26,29,34,35] and others utilized partial mouth examinations or the CPITN to define the exposure,[16,17,25,26,34,35] methods with limited sensitivity.[44] A meta-analysis of 17 observational studies of this relationship by Vergnes et al. (2007) investigated the possibility of publication bias using a funnel plot and statistical tests for asymmetry (Begg's and Egger's tests), finding no evidence of bias in reporting according to magnitude or significance of the association.[39]

Results from systematic reviews and meta-analyses of interventional studies have been mixed, with authors citing similar issues to those in the observational literature regarding heterogeneity in populations, methodology, and quality among studies. Meta-analyses reported finding sub-groups of studies for which periodontal therapy reduced risk for adverse pregnancy outcomes, including studies with populations at high risk of preterm birth,[10] high quality studies with demonstrated control of periodontal disease,[9] studies with participants with less severe periodontal disease,[45] or studies utilizing a cointervention of chlorhexidine oral rinse.[46] Several other meta-analyses, however, concluded no effect of periodontal therapy on adverse pregnancy outcomes, including two that found that the subgroup of studies with unclear or high risk of bias reduced risk for preterm birth while studies with low risk of bias did not.[47-50]

Studies of the periodontal disease and adverse pregnancy outcome relationship in HICs have important differences from those in LMICs, particularly the high prevalence of confounders such as smoking, alcohol use, chronic disease (e.g. hypertension and diabetes) and known race-specific effects (e.g. higher prevalence of periodontal disease among African Americans). Some populations in LMICs, particularly in rural areas, have very low levels of these risk factors among women of childbearing age, presenting unique opportunities to observe this epidemiologic association in the absence of important confounders. Many studies in this review included populations with low levels of these traditional risk factors, but none addressed the potential for the influence of other factors, present primarily in LMICs, such as malaria infection, helminths, or other tropical diseases, which could act as an inflammatory burden during pregnancy and confound the association of interest. Additionally, the confounding or modifying effect of yet unknown and unmeasured factors, such as a genetic hyper-inflammatory phenotype, in any setting, HIC or LMIC, cannot be ruled out and should be considered by future investigations.

Nearly all studies of this relationship, at any income level, have been conducted in hospital-based settings, introducing the risk of selection bias. The potential for selection bias to influence the measure of association in a hospital-based study is especially high in populations where a significant proportion of women deliver at home. Data suggesting how selection probabilities in hospital-based studies might be related to exposure or disease status for this relationship are unavailable. Future studies should consider the implications of selection bias, and given the difficulties in adjusting for this particular epidemiologic bias, utilize study designs and methodologies to avoid selection bias. Alternatively, studies could employ sensitivity analyses to detect the presence and estimate the magnitude and direction of any such bias for adjustment. Community-based studies in LMICs, while financially and logistically intensive, can minimize sample frame bias and other threats to validity, such as non-response or loss-to-follow-up biases.

This review had several limitations, most notably, the inability to apply a more specific definition for community-based studies, due to the varied and limited information on study, source, and target populations provided by included studies. Some studies screened by this review were ambiguous, and many did not comment, on the proportion of the population delivering at their facility, raising the possibility that our assignment of the community-based status may have included some misclassification. Classification of studies as high- or low- and middle-income is a broad categorization that ignores differences between sub-populations in these countries (e.g. across urban and rural communities) and the rapidly shifting burden of disease in LMICs. We attempted to overcome this issue by describing the relevant characteristics of populations in reviewed studies to the extent possible. Variation in study designs and epidemiologic recording systems and case definitions for periodontal disease across studies limited the comparison of results and prevented a pooled analysis.

Conclusion

Most studies exploring the maternal periodontal disease and adverse pregnancy outcome association have been conducted in hospital-based settings. In many low- and middle-income countries, a large proportion of women deliver at home or at first level primary health centers and differ in important ways from those delivering in hospitals. Only one observational study of the maternal periodontal disease and adverse pregnancy outcome association has been conducted in a community-based setting, although several other observational studies enrolled participants from multiple facilities within a single community. Our review found these studies to be widely heterogeneous in population and methodology, and their results mixed. High quality community-based trials are needed to assess the effectiveness of oral health interventions on the risk of adverse pregnancy outcomes in low- and middle-income countries.

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Table 1: Summary of community-based studies of the periodontal disease and preterm birth association conducted in low- and middle-income countries

Tier definition	Included studies	Countries	Summary of results
1. Prospective cohort studies in a home setting with a population sample	1 cohort study	Pakistan	Significant associations were found between periodontal disease and neonatal death, perinatal deaths, and stillbirth
2. Prospective cohort studies in a hospital or clinic setting	1 non-randomized trial 5 cohort studies	Brazil (n=1), Malaysia (n=2), Fiji, Jordan, Madagascar	A non-randomized trial found a borderline significant association between periodontitis and LBW among controls Four cohort studies found associations between periodontal disease, using various definitions, and PTB, LBW, or PE One cohort study found no association between periodontal disease and PTB or LBW
3. Case-control and cross-sectional studies in a hospital or clinic setting	17 case-control studies	Brazil (n=8), India (n=2), Iran (n=2), Thailand (n=2), Uganda (n=1), Vietnam (n=1), China (n=1)	Two of three case-control studies with PTB outcome found significant relationships with periodontal disease Three of four studies with LBW outcome found significant associations with periodontal disease (in one study only in women with low education Three of four studies with PE outcome found significant relationships with periodontal disease. Two of six studies considering multiple or composite outcomes found a significant relationship with periodontal disease

Chapter 3: Validation of periodontal examinations conducted by community-based oral health workers in Sarlahi District, Nepal

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Background

Periodontal diseases, including gingivitis and periodontitis, constitute a major burden of chronic disease globally.[1] Gingivitis is common in children and adults, and severe periodontitis affects 10% to 15% of adults.[2] Disadvantaged communities, in both high- and low-income countries, have higher rates of periodontal disease and limited access to oral health care, especially preventative services.[3] The majority of research on periodontal health has been conducted in high-income countries, and critical knowledge gaps about the inequities in oral health exist, including those related to the social determinants of oral health, effective community-based intervention programs for oral diseases, and the relationships between oral health and chronic disease, among other areas.[4,5]

In many low-income countries, oral health facilities, equipment, and importantly, qualified personnel, are in short supply.[6] Nepal, for example, has only 2 dentists per 100,000 population, one of the lowest ratios among South Asian countries.[7] In such contexts, shifting clinical tasks to less specialized health care workers may help alleviate the human resource demand for research or programmatic purposes. Community health workers have demonstrated the ability to safely and effectively conduct clinical diagnostic tasks, and deliver essential care, for a variety of illnesses in a home setting.[8-10] To our knowledge, no studies have evaluated the ability of community health workers to assess the clinical signs of periodontal health.

Task shifting necessitates assessment of the validity and accuracy of measures or procedures prior to wider implementation; this is especially so in measurement of clinical periodontal parameters. Over the past several decades, periodontal researchers have sought to improve data quality by designing a standardized process to assess periodontal examiners.[11-14] Validity and reliability studies have been used to determine if periodontal measurements conducted by periodontal examiners are consistent with a gold standard or within and between examiners.[15,16] Important considerations in these studies include selecting measurement indices amenable to repetition; utilizing a primary sampling unit consistent with the outcome of the main study; calculating appropriate sample size for the desired precision; reporting of the uncertainty (i.e. 95% confidence interval) of the reliability measures considered (e.g. kappa statistic); and adjusting for clustering by tooth sites within subjects if appropriate.

Given the potential benefit of extending periodontal examination to a community setting, we estimated the validity of periodontal measurements collected by community-based oral health workers relative to an experienced dentist in rural Sarlahi, Nepal.

Methods

We recruited twenty-one pregnant women <26 weeks gestation in a sub-area of Sarlahi District, Nepal between January and November 2016. These women were enrolled in the Nepal Oral Health Cohort Study (NOHCS), a community-based, prospective cohort study of periodontal disease and adverse pregnancy outcomes. Participants were identified and determined eligible using the infrastructure of a large community-based randomized trial, the Nepal Oil Massage Study (NOMS) (NCT01177111), which was operating concurrently in this study area, and actively enrolling a population-based sample of pregnant women in Sarlahi District.

Oral health worker training: Five auxiliary nurse-midwives, who completed an 18-month government certified program but had no previous experience in dentistry or clinical research, were trained in basic dental anatomy, pathology, and the procedures for periodontal examination by an experienced dentist (NA) from the Department of Dentistry, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. Training for these "community-based oral health workers" included identification of plaque and calculus, signs of gingivitis, and measurement of probing depth (PD), bleeding on probing (BOP), and distance from the cemento-enamel junction to the free gingival margin (CEJ-GM). Oral health workers were also trained in clinical research methods and ethics for human subjects research. Training lasted 3-4 weeks and included classroom instruction and practice of periodontal techniques under the guidance of the dentist.

Oral health worker assessment: All NOHCS study visits were conducted at participant's homes (Figure 1) because of the wide dispersion of households and villages across this rural community and the impracticality of bringing participants to a central location. Oral health workers and an assistant traveled to participant's homes by motorbike, carrying with them all of the equipment required to conduct the exam. After the consent process, oral health workers asked the participant where in the home they felt most comfortable having the examination. A location was selected by the oral health workers in an attempt to maximize the available natural light and participant privacy. Often examinations were conducted inside the house on a bed or the floor in dim lighting. Ideal conditions were found in households with an enclosed courtyard, allowing for the exam to be conducted outdoors on the porch or ground, providing the most natural light. Electric lighting was present in very few households, and whether examinations were conducted inside or outside, oral health workers relied on battery-powered headlamps to illuminate the mouth.

Each participant underwent a full mouth examination by one of the oral health workers, and following a fifteen-minute break and mouth rinse with water, a second examination by the dentist. Data were recorded on paper forms by a trained assistant, and electronically entered by experienced data entry operators. Periodontal measurements were made using a color Williams probe (Hu-Friedy, Chicago, IL, USA). PD was measured on six sites per tooth (disto-, mid-, and mesial- aspects of buccal and lingual surfaces) and the CEJ-GM distance on two sites per tooth (mid- buccal and lingual aspects), excluding third molars. After probing each quadrant, the presence or absence of BOP was recorded for buccal and lingual surfaces of each tooth. PD values were recorded in millimeters from 1 to 10, rounded to the next higher whole number. CEJ-GM distances were recorded similarly, with values of 0 to 10 millimeters. If the free gingiva was coronal to the CEJ, the CEJ-GM measurement was recorded as 0. Clinical attachment loss (CAL) was calculated by summing PD and the CEJ-GM distance; the CEJ-GM distance was assigned a value of 0 for distal and mesial sites, where this measure was not collected.

Statistical analysis: Basic participant characteristics were reported as percentages. Differences between periodontal characteristics, as measured by the oral health workers and the dentist, were evaluated using paired t-tests or McNemar's chi-squared tests. Percent agreement was calculated between the pooled oral health workers and each individual worker compared to the dentist for perfect agreement and considering values of PD ±1 mm as agreement. Confidence intervals (95%) for percent agreement were adjusted for clustering associated with the measurement of multiple teeth per participant using a generalized estimating equation (GEE) model. Kappa and weighted kappa (considering PD ±1 mm as agreement) statistics for PD were calculated, using tooth site as the unit of analysis, for pooled and individual oral health workers relative to the dentist. Confidence intervals (95%) for weighted and unweighted kappa statistics were also adjusted for clustering by participant using a bootstrap approach (1,000 replications). Similarly, intraclass correlation coefficients (ICC) and associated cluster-adjusted, bootstrapped 95% confidence intervals were calculated for PD, using absolute agreement and tooth site as the unit of analysis, comparing the pooled oral health workers to the dentist for perfect agreement and PD ±1 mm agreement. Sensitivity and specificity for the classification of tooth sites as PD >2 mm were calculated for pooled and individual oral health workers vs. the dentist. A multivariable GEE model was used to estimate the effect of various periodontal characteristics on agreement between the pooled oral health workers and dentist.

Ethical review: This study received ethical approved from the Institutional Review Board at Johns Hopkins Bloomberg School of Public Health (Baltimore, USA) and the Ethical Review Board of the Nepal Health Research Council (Kathmandu, Nepal).

Results

Twenty-one pregnant women <26 weeks gestation were enrolled in this study. The mean age of participants was 22 (SD: ±3) years (Table 1). A majority of women (62%) were literate, 38% had no education, 38% 1-9 years of schooling, and 24% 10 or more years. Nearly three-quarters (71%) of participants lived in a house constructed from thatch, sticks, or bamboo, with the other 29% in a house of wood, brick, or stone, and half (48%) had no access to a latrine.

All participants had 28 teeth (third molars ignored), except for three women who were missing a single tooth (Table 2). Mean probing depth (PD) was 1.6 mm (SD: 0.3) with a range of 1 to 4 mm as measured by the oral health workers, and 1.4 mm (SD: 0.2) ranging 1 to 3 mm according to the dentist, a mean difference of 0.2 mm (p=0.02) (Figure 2). When non-congruent, these absolute differences in PD were nearly universally 1 mm, and roughly equally distributed in either direction. Collectively, the oral health workers identified one woman from the total twenty-one participants with at least one site with PD ≥4 mm, although the dentist measured these sites as <4 mm and identified no other women as having any sites with PD ≥4 mm.

The mean number of sites with bleeding on probing (BOP) was 13.6 (SD: ±11.3) and 11.4 (SD: ±12.0) for the oral health workers and the dentist, respectively ($p=0.22$). Most women, 86% according to the oral health workers, and 81% according to the dentist, had at least some bleeding ($p=0.56$). The oral health workers identified two, and the dentist three, of 21 total participants as having ≥1 mm recession of the gingival margin from the CEJ. Therefore, mean clinical attachment loss (CAL) did not differ substantially from the measures of PD.

Overall percent agreement for the oral health workers relative to the dentist was 63.3% and 99.3%, for perfect and ±1 mm agreement, respectively. Percent agreement differed significantly ($p<0.001$) when stratified by PD, ranging from 62% agreement for PD=1 mm to 48% for PD=3 mm (Figure 2). For the individual oral health workers vs. the dentist, ranges of percent agreement and agreement ±1 mm were 57% to 69% and 99% to 100%, respectively. We calculated a design effect of 13.2 for the perfect agreement among the pooled oral health workers, indicating a high level of variation in PD between subjects. By individual participant, percent agreement and agreement ±1 mm ranged from 40% to 90% and 96% to 100%. Design effects for perfect percent agreement among the individual oral health workers ranged from 3.7 to 25.9.

The kappa score between the pooled oral health workers and the dentist was 0.32 (95% CI: 0.24, 0.41) for perfect agreement, and 0.85 (95% CI: 0.76, 0.93) for agreement within ±1 mm (Table 3). Kappa scores for the five individual oral health workers compared to the dentist ranged from 0.24 (95% CI: 0.06, 0.42) to 0.40 (95% CI: 0.22, 0.59) for perfect agreement, and 0.74 (95% CI: 0.67, 0.78) to 1.0 for agreement within ±1 mm (Table 4). The intraclass correlation coefficient (ICC) between the pooled oral health workers and the dentist was 0.43 (95% CI: 0.35, 0.51) for perfect agreement, and 0.94 (95% CI: 0.91, 0.98) for agreement within ±1 mm (Table 3). ICC values for the five individual oral health workers compared to the dentist ranged from 0.34 (95% CI: 0.16, 0.55) to 0.49 (95% CI: 0.31, 0.66) for perfect agreement, and 0.90 (95% CI: 0.80, 1.00) to 1.0 for agreement within ±1 mm (Table 4).

Relative to the dentist, the pooled oral health workers classified individual tooth sites as PD ≤2 mm or PD >2 mm with 50% sensitivity and 96% specificity. For the five individual oral health workers, each relative to the dentist, sensitivity ranged from 19% to 85% and specificity from 92% to 99% (Table 5). However, oral health workers classified more sites as PD >2 mm than the dentist, an average of 5.6% sites per participant vs. 2.5%. Sensitivity and specificity of BOP were 53.8% and 91.5%, respectively, for the pooled oral health workers relative to the dentist, with sensitivity ranging from 31% to 71% and specificity from 88% to 96%, for individual oral health workers (Table 6).

We modeled the relative risk (RR) of percent agreement for PD of the oral health workers relative to the dentist using a generalized estimating equation (GEE) regression model, including covariates for periodontal characteristics (Table 7). Covariates for jaw (maxilla, mandible), side (left, right), and probing depth (≤2 mm, >2 mm) were not significantly related to percent agreement. PD measurements on posterior teeth and lingual surfaces were associated with an average reduction in percent agreement of 15% (0.81, 0.90) and 10% (95% CI: 0.86, 0.95), respectively. Measurements on direct tooth site, relative to the proximal site, were associated with a 21% increase in agreement.

Discussion

Results from our study demonstrate that community-based oral health workers with 3-4 weeks training can accurately conduct periodontal examination in a low resource setting. Percent agreement, weighted kappa scores, and intraclass correlation coefficients, with an allowance of ±1 mm, exceeded 99%, 0.7, and 0.9, respectively, indicating an acceptable level of agreement. While the oral health workers tended to overestimate probing depth (PD) scores relative to the dentist, the magnitude of this over-estimation was small (0.2 mm) and unlikely to impact the population-based estimates of critical indicators. Relative to the dentist, the capacity of the oral health workers to distinguish sites with PD >2 mm was less than ideal (sensitivity of 50%); however, oral health workers demonstrated an excellent ability to discern sites with PD ≤2 mm (specificity 96%). Sensitivity and specificity for bleeding on probing (BOP) data exhibited a similar pattern to PD, but should be interpreted with caution, due to the possible influence of the first examination on the subsequent one, given the short recovery interval (15 minutes) for each participant.

A review of the periodontal literature, conducted by Hefti and Preshaw (2012), showed that only 30% of publications using the Gingival Index or Modified Gingival Index reported on examiner assessment, and nearly none discussed the possible consequences of examiner validity or reliability on the outcome of the study.[15] Studies of the association between periodontal disease and adverse pregnancy outcomes that have reported on examiner assessment typically included only one to two sentences in the methods section, without estimates of uncertainty or information on the sample size and study design utilized to collect these data. Our estimates of validity and reliability were generally comparable to those documented by similar studies, although some achieved both weighted kappas and ICCs of over 0.9.[17]

Community-based periodontal examination presents various challenges not found in a typical clinical setting, notably the absence of a high-quality light source.[18] Some variability observed in the measures of validity in this study may be attributable to the field conditions. We identified lower agreement on posterior teeth, lingual surfaces, and proximal sites, areas that may be more difficult to measure accurately in low light. Alternatively, this variability could be a result of the limited training of the oral health workers, or even normal inter-rater variability, as lower agreement for posterior, lingual, and proximal sites has also been seen in reliability studies utilizing highly trained periodontal examiners.[19,20] Decreasing agreement has been associated with increasing probing depth in other periodontal studies, and although our oral health workers measured twice as many sites with PD >2 mm, results from the regression model found a non-significant relationship between agreement for PD ≤2 mm and PD >2mm.[18,21] This analysis may have been limited by the relatively shallow pockets of participants in our study population. Bias may have also originated from oral health workers' knowledge of when the dentist was visiting (blinding was not possible for logistical reasons), leading the oral health workers to take extra time and care on each measurement, with the result of higher mean probing depths than the dentist.

A large majority of women in our study population had signs of gingivitis, indicated by the high prevalence of bleeding on probing (BOP), but very few had any gingival recession or probing depths ≥4 mm, suggestive of periodontitis. The minimal prevalence of periodontitis measured in our study may be a result of the young age of the study population, which is low even for other studies of the periodontal disease and adverse pregnancy outcome association.[22] Additionally, the small sample size of this study may have played a role; initial data from the parent study, NOHCS, indicate a prevalence of ≥1 site with PD ≥4 mm of over 8%. Our assessment of the amount of measurement error associated with the study's oral health workers may be underestimated if higher probing depths are measured with lower validity and reliability in this setting.

Although the oral heath field workers – who collected data for this validation study and the parent study, the Nepal Oral Health Cohort Study (NOHCS) – underwent an extensive training (described in the methods section above) before the start of NOHCS, this validation study was nested within NOHCS, precluding the possibility of retraining the oral health workers based upon this study's results. Sample size was restricted for logistical reasons; with additional participants we could have estimated reliability measures of intra-rater agreement for the repeated measurements of each oral health workers and inter-rater agreement between the study's five oral health workers. We prioritized validity over reliability because the oral health workers in this study had no previous experience in dentistry or clinical research. With a larger sample, we might have also measured agreement using the subject as the unit of analysis, an approach that could have yielded practical information for the parent study, which will take the subject as the primary unit of analysis. As a result of the absence of moderate or severe periodontal disease, driven in part by the small sample, the bulk of our analyses focused on discriminating between low probing depth scores, primarily 1-2 mm, which are indicative of periodontal health. This limited our ability to fully explore the capacity of the oral health workers to accurately measure the full range of clinical periodontal parameters, such as PD and CAL, and distinguish between states of disease from health.

Conclusion

Our study demonstrates that community-based oral health workers can accurately conduct periodontal examination, suggesting the potential to shift tasks away from highly trained periodontal examiners to in low resource settings. Further research is needed to assess intra- and inter-rater reliability among oral health workers, which was not measured in this study, and explore the use of oral health workers for other types of oral health assessment, such as the detection of dental caries, and in other populations.

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Table 1: Demographic characteristics of participants in the validation study

Characteristic	Frequency	Percent
Age (years)		
<20	7	33.3
20-24	11	52.4
25-29	3	14.3
Literacy		
No	8	38.1
Yes	13	61.9
Education (years)		
0	8	38.1
1-9	8	38.1
≥10	5	23.8
House construction material		
None, thatch, sticks, or bamboo	15	71.4
Wood planks, brick, or stones with mortar	6	28.6
Latrine		
No latrine	10	47.6
Brick, concrete, or pit latrine	11	52.4

Table 2: Periodontal characteristics of participants in the validation study

Characteristic	Oral health workers	Dentist	P-value
Number of teeth*			
Mean number of teeth	27.9 ± 0.36	27.9 ± 0.36	-
Bleeding on probing (BOP)			
Percent of sites BOP	13.6 ± 11.3	11.4 ± 12.0	0.22
≥1 site BOP (No. (%))	18 (85.7)	17 (81.0)	0.56
≥1 site & <10% of sites BOP (No (%))	5 (23.8)	8 (38.1)	-
≥10% & <25% of sites BOP (No (%))	8 (38.1)	5 (23.8)	-
≥25% of sites BOP (No (%))	5 (23.8)	4 (19.1)	0.56
Probing depth (PD)			
Mean PD (mm)	1.6 ± 0.3	1.4 ± 0.2	0.02
Percent of sites with PD ≥3 mm	9.3 ± 11.5	4.2 ± 6.0	0.05
≥1 site PD ≥4 mm (No (%))	1 (4.8)	0 (0.0)	-
Clinical attachment loss (CAL)~			
Mean CAL (mm)	1.6 ± 0.3	1.4 ± 0.2	0.02
≥1 site CAL ≥4 mm (No (%))	2 (9.5)	1 (4.8)	0.56

Data presented as mean ± SD unless otherwise noted

* Excluding third molars

~ Direct site only

Table 3: Intraclass correlation coefficients and kappa statistics for pooled oral health workers vs. dentist

Measure	Point estimate	95% CI
Percent agreement	63.3	57.5, 69.1
Percent agreement ±1 mm	99.3	98.8, 99.8
ICC	0.43	0.35, 0.51
ICC ±1 mm	0.94	0.91, 0.98
Kappa	0.32	0.24, 0.41
Kappa ±1 mm	0.85	0.76, 0.93

Table 4: Intraclass correlation coefficients and kappa statistics for individual oral health workers vs. dentist

Oral health worker	N[*]	Tooth sites	Percent agreement	ICC	Kappa
1	4	669	62.6 (52.7, 72.6)	0.42 (0.32, 0.52)	0.31 (0.17, 0.45)
2	4	666	59.2 (53.1, 65.3)	0.47 (0.32, 0.62)	0.30 (0.20, 0.40)
3	4	666	57.8 (44.1, 71.8)	0.34 (0.16, 0.55)	0.24 (0.06, 0.42)
4	5	834	68.6 (54.0, 83.2)	0.42 (0.29, 0.55)	0.34 (0.15, 0.52)
5	4	672	67.0 (55.5, 78.5)	0.49 (0.31, 0.66)	0.40 (0.22, 0.59)
Total	**21**				

Oral health worker	N[a]	Tooth sites	Percent agreement ±1 mm	ICC ±1 mm	Kappa ±1 mm
1	4	669	100.0 (99.5, 100.0)	1.0	1.0
2	4	666	98.8 (97.7, 99.9)	0.92 (0.83, 1.00)	0.85 (0.65, 1.00)
3	4	666	98.8 (97.4, 100.0)	0.90 (0.80, 1.00)	0.74 (0.67, 0.78)
4	5	834	99.3 (98.3, 100.0)	0.93 (0.85, 1.00)	0.79 (0.69, 0.95)
5	4	672	99.7 (99.4, 100.0)	0.97 (0.95, 1.00)	0.92 (0.79, 1.00)
Total	**21**				

Data presented as point estimate (95% CI)
[*] Number of participants assessed by both the oral health worker and dentist

Table 5: Sensitivity and specificity of probing depth (PD) >2 mm classification by individual oral health workers vs. dentist

Oral health workers	N*	Tooth sites	No. sites PD >2 mm~	Sensitivity	Specificity
1	4	669	9	55.6%	95.3%
2	4	666	24	83.3%	91.5%
3	4	666	27	38.1%	94.7%
4	5	834	33	18.5%	98.6%
5	4	672	13	84.6%	97.0%
Total	**21**				

* Number of participants assessed by both the oral health workers and dentist

~ Number of sites with PD >2 mm according to dentist's measurement

Table 6: Sensitivity and specificity of bleeding on probing (BOP) classification by individual oral health workers vs. dentist

Oral health worker	N*	Tooth sites	No. sites BOP~	Sensitivity	Specificity
1	4	669	126	71.4%	89.0%
2	4	666	78	30.8%	95.9%
3	4	666	54	66.7%	87.8%
4	5	834	108	41.7%	91.3%
5	4	672	30	60.0%	93.5%
Total	**21**				

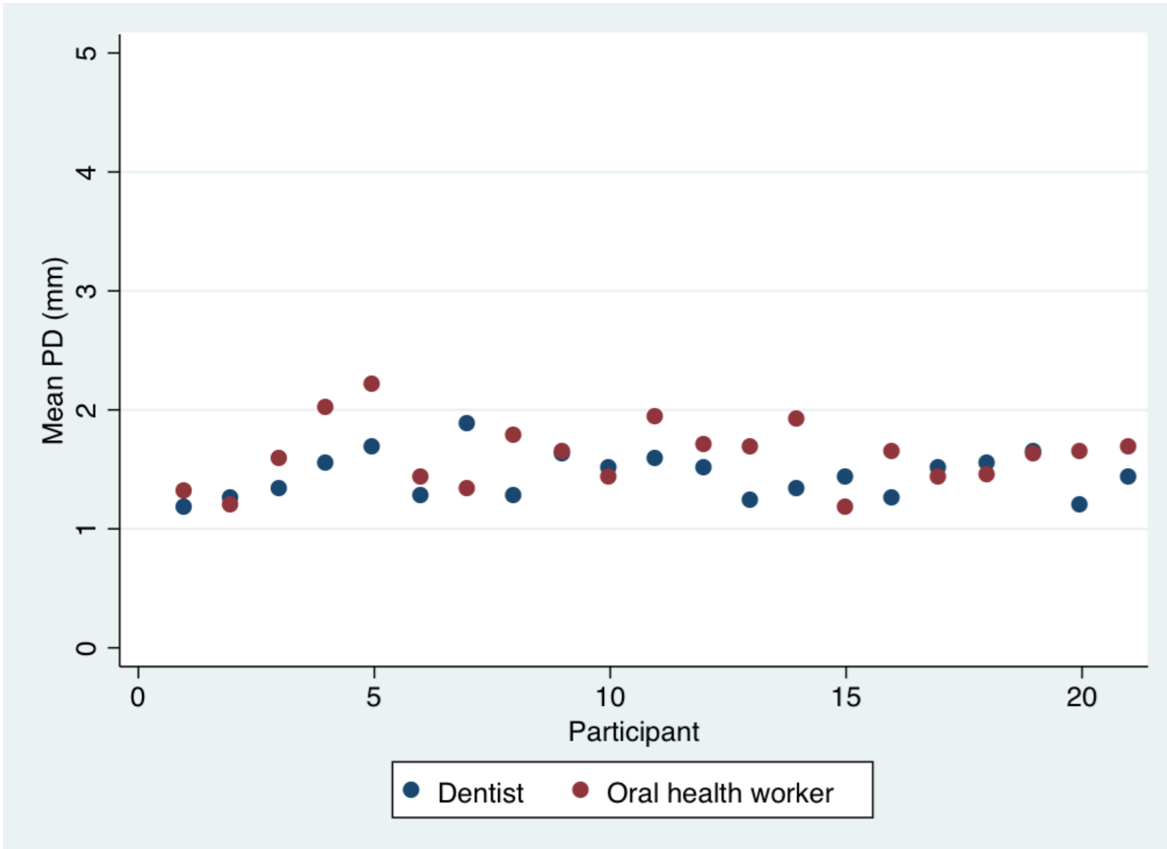
* Number of participants assessed by both the oral health worker and dentist
~ Number of sites with BOP according to dentist's measurement

Table 7: Relationships between probing depth (PD) agreement and periodontal characteristics using a multivariable GEE model

Variables	RR	95% CI
Jaw		
Mandible	0.96	0.92, 1.00
Maxilla	Ref	-
Side		
Right	1.01	0.97, 1.06
Left	Ref	-
Position		
Posterior	0.85	0.81, 0.90
Anterior	Ref	-
Surface		
Lingual	0.90	0.86, 0.95
Facial	Ref	-
Site		
Direct	1.21	1.15, 1.28
Proximal	Ref	-
Probing depth		
>2 mm	0.85	0.70, 1.05
≤2 mm	Ref	-

Figure 1 A & B: Community-based oral health workers conducting periodontal examinations participant homes

Figure 2: Mean probing depth (PD) measured by individual oral health workers and dentist for each participant



Chapter 4: Oral hygiene practice, care-seeking, knowledge, and periodontal disease status among women in the Terai region of Nepal

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Background

Periodontal disease includes a group of inflammatory conditions, typically initiated by oral bacteria, progressing from reversible accumulation of plaque and inflammation of gingival tissue (gingivitis) to irreversible breakdown of the supportive tissues of the teeth and eventually tooth loss (periodontitis).[1] Globally, gingivitis is common and severe periodontitis affects 10% to 15% of adult populations.[2] Risk factors for periodontal disease include older age, poor oral hygiene, tobacco use, alcohol consumption, stress, malnutrition, and diabetes mellitus and other chronic diseases.[3] Associations have been observed between periodontal disease and distal factors such as income and education, urban/rural location, race, and ethnicity.[4] Periodontal disease has been implicated as a potential cause of systemic conditions, such as cardiovascular disease and adverse pregnancy outcomes.[5]

Although periodontal health is recognized as an important component of general well-being, oral health remains neglected in many low- and middle-income countries and among high-risk and underserved sub-populations in some high-income countries.[6,7] In many low-income countries, oral health facilities, equipment, and personnel are in short supply, severely limiting access to care, especially preventative services.[7] Nepal, for example, has only 2 dentists per 100,000 population, one of the lowest ratios among South Asian countries.[8] Few studies have assessed the oral health and oral hygiene practices of adult Nepalis. A review of four surveys conducted in the 1980s concluded that Nepal ranked among the bottom 15% of countries in terms of periodontal conditions.[9] A more recent national survey (2004) showed some improvement; Community Periodontal Index of Treatment Needs (CPITN) scores among 15-16 year-olds were 26% periodontal health (score 0), 8% bleeding on probing (BOP) (score 1), 61% BOP and calculus (score 2), 5% probing depth 4-5 mm (score 3), and 0% PD $\geq$ 6 mm (score 4), and among 35-44 year-olds, 7% periodontal health (score 0), 3% BOP (score 1), 27% BOP and calculus (score 2), 48% PD 4-5 mm (score 3), and 16% PD $\geq$ 6 mm (score 4).[10-12]

The oral health status of pregnant women in low-resource communities such as Nepal has not been well characterized. This sub-population is also of specific interest given previously documented associations between poor oral health and adverse pregnancy outcomes.[13,14] In this study, we explored relationships between demographic characteristics, oral hygiene practices, care-seeking, knowledge, and periodontal disease among pregnant women in the Terai region of Nepal.

Methods

We recruited pregnant women <26 weeks gestation in a sub-area of Sarlahi District, Nepal between January and October 2016. These women were enrolled in the Nepal Oral Health Cohort Study (NOHCS), a community-based, prospective cohort study of periodontal disease and adverse pregnancy outcomes. Participants were identified and determined eligible using the infrastructure of a large community-based randomized trial, the Nepal Oil Massage Study (NOMS) (NCT01177111), which was actively enrolling a population-based sample of pregnant women in this study area.

Oral health examination: Oral health examinations were performed by five auxiliary nurse-midwives, with no previous experience in dentistry or clinical research, who were trained as "community-based oral health workers" for this study by an experienced dentist (NA) at the Department of Dentistry, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. Training for the oral health workers included identification of plaque and calculus, signs of gingivitis, and measurement of probing depth (PD), bleeding on probing (BOP), and distance from the cemento-enamel junction (CEJ) to the free gingival margin (CEJ-GM). Oral health field workers were also trained in clinical research methods and ethics for human subjects research. Training lasted 3-4 weeks and included classroom instruction and practice of periodontal techniques under the guidance of the dentist. We estimated the validity of PD measurements of the oral health workers relative to the dentist and found that percent agreement, weighted kappa scores, and intraclass correlation coefficients, with an allowance of PD ±1 mm, exceeded 99%, 0.7, and 0.9, respectively, indicating an acceptable level of agreement.

Periodontal measurements were made using a color Williams probe (Hu-Friedy, Chicago, IL, USA). PD was measured on six sites per tooth (disto-, mid-, and mesial- aspects of buccal and lingual surfaces) and the CEJ-GM distance on two sites per tooth (mid- buccal and lingual aspects), excluding third molars. After probing each quadrant, the presence or absence of BOP was recorded for buccal and lingual surfaces of each tooth. PD values were recorded in millimeters from 1 to 10, rounded to the next higher whole number. CEJ-GM distances were recorded similarly, with values of 0 to 10 millimeters. If the free gingiva was coronal to the CEJ, the CEJ-GM measurement was recorded as 0. Clinical attachment loss (CAL) was calculated by summing the PD and CEJ-GM distance; the CEJ-GM distance was assigned a value of 0 for distal and mesial sites, where this measure was not collected. All scores were recorded on paper forms by a trained assistant, and electronically entered by experienced data entry operators.

Clinical periodontal disease status was categorized based upon our interest in the condition as an exposure with potential for systemic effects, particularly adverse pregnancy outcomes.[15] We defined gingivitis as at least one site with PD 3 mm and BOP but no sites PD ≥4 mm and periodontitis as at least one site with PD ≥4 mm.[16,17] For many of our analyses, we divided participants into those with periodontal health and those with either gingivitis or periodontitis, who we collectively referred to as having "periodontal disease."

Oral hygiene questionnaire: Data on participant demographics, oral hygiene practice, care-seeking, knowledge, and other characteristics were collected in the home, through a series of questionnaires administered over the course of pregnancy.

Statistical analysis: Descriptive bivariate analyses between participant characteristics and the outcome, periodontal disease, were evaluated using t-tests and logistic regression for continuous and binary/categorical variables, respectively. We ran a series of logistic regression multivariable models, sequentially including risk factor variables from four broad domains: maternal characteristics, oral hygiene behaviors, oral health knowledge and attitudes, and socioeconomic characteristics. Covariates were selected for inclusion in these regression models by examining bivariate relationships with periodontal disease status using a cutoff of $p<0.10$. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated. All statistical analyses were performed in STATA 14.2 (StataCorp, College Station, TX, USA).

Ethical review: This study received ethical approved from the Institutional Review Board at Johns Hopkins Bloomberg School of Public Health (Baltimore, USA) and the Ethical Review Board of the Nepal Health Research Council (Kathmandu, Nepal).

Results

A total of 1,457 pregnant women were enrolled in this study between January 11, 2016 and November 26, 2016. Of these participants, 32 were lost to follow-up after the periodontal examination and, therefore, provided data on their periodontal health but not on oral health risk factors for this analysis.

Periodontal disease status: The majority of women (84%) had all 28 teeth (ignoring third molars) (Table 1). Most participants (79%) had at least one site with BOP, and participants averaged 10% of sites with BOP, the equivalent of 17 tooth sites (median 9) per participant. Mean PD was 1.7 mm (SD: 0.3) and max PD ranged from 2 mm to 7 mm. Nine percent of participants had at least 1 site with PD ≥4 mm, although very few participants (0.7%) had sites with PD ≥5 mm. Mean CAL was equivalent to mean PD, and nearly all of CAL ≥4 mm was due to pocketing, indicating very little recession of the gingiva in this population. Only 13% of participants had at least one site with recession.

Almost half of all participants (47%) fit the definition of periodontal health, 45% had gingivitis, and 9% periodontitis. Among women with gingivitis or periodontitis (53%), participants averaged 16% of sites with BOP, with the highest quartile having BOP at 23% of sites (Figure 1). In the same group, mean PD and mean CAL were slightly higher than among all women, at 1.8 mm (Figure 2). Categorizing participants according to the Community Periodontal Index of Treatment Needs (CPITN), 20% of participants had periodontal health (score 0); 71% BOP or BOP and calculus (scores 1 & 2);[1] 8% PD 4-5 mm (score 3); and <1% PD ≥6 mm (score 4) (Table 2).[18,19]

Oral pain status: Very few participants (7%, n=107) reported having any oral pain (Table 3). Of those with pain, it was typically mild (84%), although 16% (n=17) reported

[1] Presence of calculus was not assessed by this study.

moderate or severe pain. Participants characterized their pain experience as toothache (47%), loose tooth (17%), sore or bleeding gums (28%), lesions in the mouth (11%), and jaw pain (23%) (multiple responses possible). Treatment sought for pain was typically increased teeth brushing or gargling with warm salt water. Of those that used medicine to treat pain, 76% of participants could not identify what type of medicine (n=13) (multiple responses possible). Only 9% (n=10) of these participants sought care from a dentist. One-quarter (25%) of participants reported having seen blood at some point in their life when cleaning their teeth, and almost half of those women (47%) saw blood within in the last week.

Demographic characteristics: Average participant age was 23.1 (SD: 4.7), and the mean gestational age of pregnant women at enrollment was 14 weeks, ranging from 6 to 25 weeks (Table 4). About two-thirds (64%) of women had a normal BMI, 30% were underweight, and only 6% overweight or obese. Roughly three-quarters of participants (72%) had at least one previous pregnancy, while 28% of women had not been pregnant before. Literacy among the study population was low (47%) and more than half of women had never attended school (54%). A majority of women lived in homes constructed of thatch, sticks, or bamboo (62%), versus wood planks, brick, or stone (38%). Women were likely to have some electricity available in the home (92%). Nearly all women had access to a well for drinking water (99%). Almost half of women had no access to a latrine (43%). Age, gravidity, electricity at home, house construction material, roof construction material, and type of latrine were associated with periodontal disease at the $p<0.05$ level. Literacy and education were associated with disease status at the $p<0.1$

level. Most notably, disease was more common in women who were older (mean difference 0.8 years, 95% CI: 0.3, 1.3) and less common in women who had no previous pregnancies (OR 0.78, 95% CI: 0.61, 0.99), had a house constructed with wood, brick, or stone (OR 0.71, 95% CI: 0.58, 0.88), or had access to a latrine (OR 0.71, 95% CI: 0.57, 0.87). Several characteristics known from previous studies to be associated with periodontal disease are not listed in Table 4 because the prevalence of these factors was reported at or near 0%, for example, smoking and other tobacco use, alcohol use, and hypertension.

Dental hygiene behaviors: Nearly all participants reported teeth cleaning, most only once per day (73%) and in the morning (99%) (Table 5). More than three quarters (78%), however, indicated that, optimally, a person should clean their teeth twice or more per day. Average teeth cleaning time was 10 (median = 5) minutes. Three-quarters (74%) of participants used a toothbrush, and a large proportion also reported using datiwan (दतिवन) (43%), a local teeth cleaning instrument fashioned from twigs of a variety trees (multiple responses possible). We identified at least 18 species of tree – including bamboo, neem, Indian rosewood, mulberry, and guava – that are used for datiwan in this community. Datiwan use was much more common among families originating in the plains region of Nepal (Madeshi ethnic group), where almost half of women (46%) reported using datiwan, than the hills region (Pahadi group), where only 8% reported use (OR 10.51, 95% CI: 5.07, 21.77). More than half of participants (58%) used toothpaste, 16% toothpowder, and 28% neither toothpaste nor toothpowder (multiple responses possible). Of women that used toothpaste, 55% had a toothpaste brand that contained fluoride. Dental floss and oral rinse use were nearly non-existent (<1%). Very few women reported changing any of their dental hygiene behaviors at the start of their current pregnancy. In general, these dental hygiene characteristics were not strongly associated with periodontal disease, although, at the $p<0.1$ significance level, periodontal disease was more common in those who used datiwan (OR 1.20, 95% CI: 0.98, 1.48) and less common among those who used a toothbrush (OR 0.79, 95% CI: 0.62, 1.00). Interestingly, women who reported having increased their frequency of teeth cleaning during their current pregnancy were less likely to have periodontal disease, relative to those who did not make this change in behavior (OR 0.59, 95% CI: 0.34, 1.03), although the number of women reporting this change was small (n=54; 4% of participants).

Dental health care seeking behaviors: While the overwhelming majority of participants (88%) had never visited a dentist, those that had sought professional care (12%, n=171) most often indicated that doing so was prompted by toothache (55%) or dental caries (62%) (multiple responses possible) (Table 6). Barriers to visiting a dentist included not knowing about dentists (18%) or where to seek care (16%), but a large proportion also indicated there was no need for them to visit a dentist (82%) (multiple responses possible). Commonly reported sources of dental health information were family (78%), radio (54%), school (46%), friends (32%), and television (15%). At the $p<0.1$ significance level, the likelihood of periodontal disease was lower among women who reported receiving dental health information from their family (OR 0.80, 95% CI: 0.62, 1.03) or from television (OR 0.75, 95% CI: 0.56, 1.00).

Dental health attitudes: Participants reported many different reasons why they cleaned their teeth (Table 7). Most frequently mentioned barriers to more frequent cleaning included never being taught to clean their teeth (36%), not thinking additional teeth cleaning was necessary (37%), too much bother (32%), teeth are not dirty (18%), not enough time (18%), and no one else is doing so around me (15%) (multiple responses possible). At the $p<0.05$ level, periodontal disease was less common among with women who said that their teeth are not dirty (OR 0.61, 95% CI: 0.46, 0.80) and that teeth cleaning doesn't help (OR 0.53, 95% CI: 0.36, 0.78). At the $p<0.1$ level, periodontal disease was more common among women who said that teeth cleaning being a bother prevented them from cleaning their teeth more often (OR 1.23, 95% CI: 0.98, 1.53).

Multivariable analysis: For each year of age, the odds of periodontal disease increased significantly by 4% (aOR 1.04, 95% CI: 1.01, 1.07) (Table 8). Participant self-report that their teeth or gums were not dirty, as a reason for why participants did not clean their teeth more often, was significantly associated with reduced odds of periodontal disease (aOR 0.70, 95% CI: 0.51, 0.97). Having a house constructed of wood, brick, or stone, relative to plastic, thatch, or grass, was also associated with a reduced odds of periodontal disease (OR 0.78, 95% CI: 0.62, 0.99).

Discussion

We found approximately half of women in this population to have either gingivitis or periodontitis. Although bleeding on probing was highly prevalent, very few women had signs of periodontitis. Participants had minimal recession, and clinical attachment loss

(CAL) estimates, in both women with and without disease, were driven primarily by probing depth. This may be a result of the young age distribution of the population. Community Periodontal Index of Treatment Needs (CPITN) scores from our study fit with the disease burden seen in the most recent national survey of periodontal disease in Nepal.[10]

Age was positively associated with periodontal disease, while self-report of teeth not requiring cleaning and solid house construction material, a basic indicator of socioeconomic status, were associated with periodontal health. Many common risk factors for periodontal disease, such smoking, alcohol use, and hypertension and other chronic diseases were low or nonexistent in this population. Similarly, the racial and ethnic composition of the study population was relatively homogenous, primarily divided across two ethnic groups (Pahadi and Madeshi) indigenous to Nepal. Risk factors for poor oral health that were prevalent in our population included rural location, low-socioeconomic status, and poor oral hygiene, specifically that women typically only cleaned their teeth once per day (often with datiwan, rather than a toothbrush), few used fluorinated toothpaste, almost none flossed or used oral rinse, and professional dental health care was rare.[20-22]

Some oral hygiene habits identified in this study were described similarly elsewhere, such as the practice of cleaning teeth only once per day (typically in the morning), but other habits were different, such as the high prevalence of datiwan use in our population, likely driven by behaviors common to the Madeshi ethnic group and the Terai region.[23-25]

A large majority of women in this community had never visited a dentist or received any dental care.[23] A higher proportion of participants from this study reported having pain due to bleeding or swollen gums (relative to tooth pain) compared to those in an urban population in Eastern Nepal.[24]

Although available confounders were controlled for in this analysis, important underlying causes of periodontal disease were not represented, including systemic conditions, such as diabetes mellitus or psychosocial factors, such as stress.[3] Although chronic diseases are likely under-diagnosed in this rural population, we suspect the prevalence of chronic disease to be low, given previous studies of risk factors in this population, and the young age of women in this study.[26] Undernutrition was not directly considered in the analysis, but was likely prevalent among women in the study population.[27]

We selected our definition of periodontal disease to reflect our interest in the condition as an exposure for adverse pregnancy outcomes, such as preterm birth and low birth weight. Probing depth served as an indicator of the mucosal surface area accessible to microorganisms, while bleeding on probing reflected the inflammatory condition of the tissue. Beck and Offenbacher (2002) demonstrated that individuals with extensive attachment loss might have few or no deep pockets or bleeding on probing, and individuals with almost no attachment loss can exhibit pocketing and bleeding.[15] They proposed that when considering periodontal disease as an exposure for a systemic, contemporaneous outcome, such as C-reactive protein levels or acute myocardial infarction, attachment loss, as a historical marker for cumulative tissue and bone destruction, may not be the most appropriate measure. We believe that the inflammatory processes that precipitate early spontaneous delivery represent such an outcome, thus informing our exposure definition.

This study had several limitations. Attachment loss, a common measure of periodontal disease, was not included in our outcome definition for reasons discussed above. Other important indicators of periodontal disease, such as gingival and plaque scores, were not measured due to visit time constraints and variability in exam conditions, particularly in the amount of lighting. Although the validity of PD measurements for each community-based oral health worker was assessed relative to a dentist, reliability between or within the oral health workers was not evaluated.

Conclusion

This study found half of women of childbearing age to have signs of gingivitis or periodontitis. Oral hygiene behaviors were less frequent and varied from recommended practices and access to dental health services was uncommon. Age and lower socioeconomic status were among the risk factors for periodontal disease. These findings were consistent with the burden of periodontal disease measured by other studies in Nepal, although some important differences were identified in this population, including the prevalent use of datiwan for teeth cleaning. [12,25] Data from this study will allow for evaluation of the role of periodontal disease in adverse pregnancy outcomes, such as preterm birth and low birth weight. Future studies could describe in further detail the severity and prevalence of periodontal disease, for example, by utilizing gingival and plaque indices, and the effectiveness of community-based interventions to prevent oral disease in women and mothers in Nepal.

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Table 1: Periodontal characteristics of participants in the oral hygiene study

Characteristic	No. (%)
Number of teeth*	
Mean number of teeth (mean ± SD)	27.7 ± 0.8
Periodontal health, gingivitis, or periodontitis	
Health (All sites either PD <3 mm or PD=3 mm & no BOP)	681 (46.7)
Gingivitis/Periodontitis	776 (53.3)
- Gingivitis (≥1 site with PD 3 mm & BOP, but no sites PD ≥4 mm)	651 (44.7)
- Periodontitis (≥1 site with PD ≥4 mm)	125 (8.6)
Bleeding on probing (BOP)	
Percent of sites BOP (mean ± SD)	10.2 ± 12.2
≥1 site BOP	1,154 (79.2)
≥1 site & <10% of sites BOP	623 (42.8)
≥10% & <25% of sites BOP	359 (24.6)
≥25% of sites BOP	172 (11.8)
Localized gingivitis (PD ≤3 mm & BOP present but <10%)	577 (39.6)
Generalized gingivitis (PD ≤3 mm & BOP ≥10%)	458 (31.4)
BOP & periodontitis (PD ≥4 mm)	119 (8.2)
Probing depth (PD)	
Mean PD (mm) (mean ± SD)	1.7 ± 0.3
Mean PD at direct sites (mm) (mean ± SD)	1.5 ± 0.3
Percent of sites PD ≥4 mm (mean ± SD)	0.2 ± 1.0
≥1 site PD ≥3 mm	1,220 (83.7)
≥3 sites PD ≥3 mm	1,023 (70.2)
≥1 site PD ≥4 mm	125 (8.6)
≥3 sites PD ≥4 mm	40 (2.7)
≥1 site PD ≥5 mm	10 (0.7)
≥3 sites PD ≥5 mm	3 (0.2)
Percent of PD ≥4 mm sites with BOP (mean ± SD)	42.9 ± 44.1
Clinical attachment loss (CAL)~	

Mean CAL (mm) (mean ± SD)	1.7 ± 0.3
Mean CAL at direct sites (mm) (mean ± SD)	1.5 ± 0.3
Percent of sites CAL ≥4 mm (mean ± SD)	0.3 ± 1.2
≥1 site recession ≥1 mm	184 (12.6)
≥1 site CAL ≥4 mm	206 (14.1)
≥3 site CAL ≥4 mm	72 (4.9)
≥1 site CAL ≥5 mm	65 (4.5)
≥3 site CAL ≥5 mm	14 (1.0)
≥1 site CAL ≥6 mm	21 (1.4)
≥3 site CAL ≥6 mm	3 (0.2)
Percent of CAL ≥4 mm due to pocketing (mean ± SD)	99.9 ± 0.5
Percent of CAL ≥4 mm due to recession (mean ± SD)	0.1 ± 0.5
Percent of CAL ≥4 mm sites with BOP (mean ± SD)	36.3 ± 41.4
Number of diseased sites (PD 3 mm & BOP or PD ≥4 mm)[+]	
0 sites	681 (46.7)
1 site	135 (9.3)
2-5 sites	293 (20.1)
>5 sites	348 (23.9)

[*] Excluding third molars

[~] The cemento-enamel junction to gingival margin distance was only measured for the direct site on the buccal and lingual surfaces. In the calculation of CAL, a value of 0 was assumed for the CEJ-GM distance at the distal and mesial sites

[+] Levels of this variable were determined by stratifying the number of diseased sites into quartiles

Table 2: Community periodontal index (CPI) scores from various studies in Nepal

Study	Date	Age-group (years)	No signs (Score 0)	Gingival bleeding (Score 1)	Gingival bleeding + calculus (Score 2)	Shallow periodontal pockets: 4–5 mm (Score 3)	Deep periodontal pockets: ≥ 6 mm (Score 4)
WHO	2004	15-16	26	8	61	5	0
WHO	2004	35-44	0	0	28	38	34
NOHCS	2016	15-41	20	71*		8	<1

Data presented as % of participants in each CPI category
* Values for scores 1 & 2 were summed because calculus was not measured in this study

Table 3: Oral pain status of participants

Characteristic	All	Periodontal health	Periodontal disease	OR (95% CI)*
Current oral pain status				
None	1317 (92.5)	625 (93.7)	692 (91.4)	Ref
Mild	90 (6.3)	37 (5.5)	53 (7.0)	1.29 (0.84, 2.00)
Moderate or severe	17 (1.2)	5 (0.7)	12 (1.6)	2.17 (0.76, 6.19)
Type of pain~				
Toothache	50 (46.7)	20 (47.6)	30 (46.2)	0.94 (0.43, 2.05)
Loose tooth	18 (16.8)	6 (14.3)	12 (18.5)	1.36 (0.47, 3.95)
Sore or bleeding gums	30 (28.0)	10 (23.8)	20 (30.8)	1.42 (0.59, 3.44)
Lesions in the mouth	12 (11.2)	5 (11.9)	7 (10.8)	0.89 (0.26, 3.02)
Jaw pain	25 (23.4)	8 (19.0)	17 (26.2)	1.51 (0.58, 3.89)
Treatment sought for pain~				
Brushing	48 (44.9)	20 (47.6)	28 (43.1)	0.83 (0.38, 1.82)
Medicine	20 (18.7)	10 (23.8)	10 (15.4)	0.58 (0.22, 1.55)
Gargle with warm salt water	40 (37.4)	18 (42.9)	22 (33.8)	0.68 (0.31, 1.52)
Change eating or drinking habits	16 (15.0)	5 (11.9)	11 (16.9)	1.51 (0.48, 4.70)
Visited a health practitioner	19 (17.8)	10 (23.8)	9 (13.8)	0.51 (0.19, 1.40)
Other	20 (18.7)	7 (16.7)	13 (20.0)	1.25 (0.45, 3.45)
Saw blood when cleaning teeth (ever)+				
No	1072 (75.3)	553 (82.8)	519 (68.7)	N/A
Yes	352 (24.7)	115 (17.2)	237 (31.3)	N/A
Saw blood when cleaning teeth (in last week)+				
No	185 (53.5)	79 (71.2)	106 (45.1)	N/A
Yes	161 (46.5)	32 (28.8)	129 (54.9)	N/A
Clench or grind teeth while sleeping				
No	1357 (95.2)	638 (95.5)	719 (95.0)	Ref
Yes	68 (4.8)	30 (4.5)	38 (5.0)	1.12 (0.69, 1.84)
Wake up with tired jaws				

No	1331 (93.4)	625 (93.6)	706 (93.3)	Ref
Yes	94 (6.6)	43 (6.4)	51 (6.7)	1.05 (0.69, 1.60)

Data presented as No. (%) unless otherwise noted

* Unadjusted odds ratio and 95% confidence interval as appropriate

~ Multiple responses possible

\+ Relationship not evaluated because bleed on probing is considered in the periodontal disease outcome definition

Table 4: Demographic characteristics of participants in the oral hygiene study

Characteristic	All	Periodontal health	Periodontal disease	Mean difference / OR (95% CI)*
Maternal age				
Year (mean, ± SD)	23.1 ± 4.7	22.7 ± 4.4	23.5 ± 4.8	0.8 (0.3, 1.3)
Maternal age (years)				
<18	158 (10.8)	87 (12.8)	71 (9.1)	0.69 (0.50, 0.96)
18-<35	1271 (87.2)	583 (85.6)	688 (88.7)	Ref
≥35	28 (1.9)	11 (1.6)	17 (2.2)	1.31 (0.61, 2.82)
Maternal height				
Cm (mean, ± SD)	150.8 ± 5.5	151.1 ± 5.3	150.7 ± 5.6	-0.4 (-1.0, 0.2)
Maternal weight				
Kg (mean, ± SD)	45.8 ± 7.1	46.0 ± 7.1	45.7 ± 7.1	-0.3 (-1.0, 0.5)
Maternal BMI				
Underweight	431 (29.6)	196 (28.8)	235 (30.3)	1.08 (0.86, 1.36)
Normal weight	935 (64.2)	443 (65.1)	492 (63.4)	Ref
Overweight or obese	91 (6.2)	42 (6.2)	49 (6.3)	1.05 (0.68, 1.62)
Ethnic group				
Hills (Pahadi)	107 (7.3)	44 (6.5)	63 (8.1)	Ref
Plains (Madeshi)	1350 (92.7)	637 (93.5)	713 (91.9)	0.78 (0.52, 1.17)
Gravidity				
First pregnancy	405 (27.8)	210 (30.8)	195 (25.1)	0.78 (0.61, 0.99)
1-3 previous pregnancies	873 (59.9)	398 (58.4)	475 (61.2)	Ref
≥4 previous pregnancies	179 (12.3)	73 (10.7)	106 (13.7)	1.22 (0.88, 1.69)
Maternal literacy				
No	782 (53.7)	347 (51.0)	435 (56.1)	Ref
Yes	675 (46.3)	334 (49.0)	341 (43.9)	0.81 (0.66, 1.00)
Maternal education (years)				
0	783 (53.8)	345 (50.7)	438 (56.5)	Ref
1-9	408 (28.0)	202 (29.7)	206 (26.6)	0.80 (0.63, 1.02)

≥10	265 (18.2)	134 (19.7)	131 (16.9)	0.77 (0.58, 1.02)
Electricity				
No	113 (7.8)	41 (6.0)	72 (9.3)	Ref
Yes	1344 (92.2)	640 (94.0)	704 (90.7)	0.63 (0.42, 0.93)
House construction material				
None, thatch, sticks, or bamboo	899 (61.7)	391 (57.4)	508 (65.5)	Ref
Wood planks, bricks, or stone	558 (38.3)	290 (42.6)	268 (34.5)	0.71 (0.58, 0.88)
House roof material				
None, plastic, thatch, or grass	112 (7.7)	42 (6.2)	70 (9.0)	Ref
Tile/tin/concrete	1345 (92.3)	639 (93.8)	706 (91.0)	0.66 (0.45, 0.99)
Latrine				
No latrine	626 (43.0)	262 (38.5)	364 (46.9)	Ref
Brick, concrete, or pit latrine	831 (57.0)	419 (61.5)	412 (53.1)	0.71 (0.57, 0.87)

Data presented as No. (%) unless otherwise noted

* T-test or unadjusted odds ratio and 95% confidence interval as appropriate

Table 5: Dental hygiene behaviors of participants

Characteristic	All	Periodontal health	Periodontal disease	Mean difference / OR (95% CI)*
Cleaning frequency (times per day)				
1	1034 (72.7)	478 (71.6)	556 (73.6)	Ref
≥2	389 (27.3)	190 (28.4)	199 (26.4)	0.90 (0.71, 1.14)
Cleaning frequency (times per week)				
1-6	56 (3.9)	19 (2.8)	37 (4.9)	Ref
7-13	1152 (80.9)	543 (81.3)	609 (80.6)	0.58 (0.33, 1.01)
≥14	216 (15.2)	106 (15.9)	110 (14.6)	0.53 (0.29, 0.98)
Cleaning timing~				
Morning	1412 (99.2)	664 (99.4)	748 (99.1)	0.64 (0.19, 2.21)
Afternoon	174 (12.2)	86 (12.9)	88 (11.6)	0.89 (0.65, 1.22)
Evening	292 (20.5)	137 (20.5)	155 (20.5)	1.00 (0.77, 1.29)
After meals	240 (16.8)	114 (17.1)	126 (16.6)	0.97 (0.73, 1.28)
After sweets	16 (1.1)	8 (1.2)	8 (1.1)	0.88 (0.33, 2.36)
Cleaning duration				
Minutes (mean ± SD)	9.6 ± 10.3	9.9 ± 10.4	10 ± 10.2	0.2 (-1.0, 1.1)
Cleaning duration (mins)				
1-2	90 (6.3)	43 (6.5)	47 (6.2)	Ref
3-10	1075 (75.8)	512 (77.1)	563 (74.6)	1.01 (0.65, 1.55)
11-29	105 (7.4)	47 (7.1)	58 (7.7)	1.13 (0.64, 1.99)
≥30	149 (10.5)	62 (9.3)	87 (11.5)	1.28 (0.76, 2.17)
Instrument use~				
Toothbrush	1047 (73.5)	507 (75.9)	540 (71.3)	0.79 (0.62, 1.00)
Datiwan	628 (43.1)	277 (40.7)	351 (45.2)	1.20 (0.98, 1.48)
Finger	212 (14.9)	103 (15.4)	109 (14.4)	0.92 (0.69, 1.24)
Brush replacement frequency (months)				
1-2	721 (69.7)	354 (71.5)	367 (68.1)	Ref
3-6	277 (26.8)	120 (24.2)	157 (29.1)	1.26 (0.95, 1.67)

≥7	36 (3.5)	21 (4.2)	15 (2.8)	0.69 (0.35, 1.36)
Dentifrice use (at least once per week)~				
Toothpaste	820 (57.5)	398 (59.6)	422 (55.7)	0.85 (0.69, 1.06)
Danta munjhan powder	229 (16.1)	111 (16.6)	118 (15.6)	0.92 (0.70, 1.23)
Charcoal	41 (2.9)	19 (2.8)	22 (2.9)	1.02 (0.55, 1.91)
Other	55 (3.9)	24 (3.6)	31 (4.1)	1.15 (0.67, 1.97)
Fluoride in toothpaste				
No	457 (42.8)	225 (42.7)	232 (43.0)	Ref
Yes	585 (54.8)	288 (54.6)	297 (55.0)	1.00 (0.78, 1.28)
Don't know	25 (2.3)	14 (2.7)	11 (2.0)	0.76 (0.34, 1.71)
New behaviors adopted during pregnancy~				
More teeth cleaning	54 (3.8)	32 (4.8)	22 (2.9)	0.59 (0.34, 1.03)
Less teeth cleaning	5 (0.4)	3 (0.4)	2 (0.3)	0.59 (0.10, 3.52)
New instrument	28 (2.0)	11 (1.6)	17 (2.2)	1.37 (0.64, 2.95)
New dentifrice	8 (0.6)	5 (0.7)	3 (0.4)	0.53 (0.13, 2.22)

Data presented as No. (%) unless otherwise noted

* T-test or unadjusted odds ratio and 95% confidence interval as appropriate

~ Multiple responses possible

Table 6: Dental health care seeking behaviors of participants

Characteristic	All	Periodontal health	Periodontal disease	OR (95% CI)*
Dentist visits over lifetime				
0	1253 (88.0)	579 (86.7)	674 (89.2)	Ref
1	75 (5.3)	36 (5.4)	39 (5.2)	0.93 (0.58, 1.48)
≥2	96 (6.7)	53 (7.9)	43 (5.7)	0.70 (0.46, 1.06)
Reason for last dentist visit~				
Regular check-up	26 (15.2)	11 (12.4)	15 (18.3)	1.59 (0.68, 3.69)
Tooth ache	94 (55.0)	51 (57.3)	43 (52.4)	0.82 (0.45, 1.50)
Gum soreness or bleeding	20 (11.7)	10 (11.2)	10 (12.2)	1.10 (0.43, 2.79)
Dental caries	106 (62.0)	56 (62.9)	50 (61.0)	0.92 (0.50, 1.71)
Other	32 (18.7)	14 (15.7)	18 (22.0)	1.51 (0.69, 3.27)
Treatment at last dentist visit~				
Regular check-up	75 (43.9)	39 (43.8)	36 (43.9)	1.00 (0.55, 1.84)
Filling or crown	31 (18.0)	24 (27.0)	7 (8.4)	0.25 (0.10, 0.62)
Tooth extraction	82 (47.7)	43 (48.3)	39 (47.0)	0.95 (0.52, 1.73)
Prescribed medicine	148 (86.0)	76 (85.4)	72 (86.7)	1.12 (0.47, 2.66)
Prescribed oral rinse	52 (30.2)	21 (23.6)	31 (37.3)	1.93 (1.00, 3.74)
Barriers to visiting the dentist~				
No need to visit a dentist	1165 (81.8)	557 (83.4)	608 (80.3)	0.81 (0.62, 1.07)
Don't know about dentists	258 (18.1)	118 (17.7)	140 (18.5)	1.06 (0.81, 1.39)
Don't know where to find a dentist	225 (15.8)	102 (15.3)	123 (16.2)	1.08 (0.81, 1.43)
Travel to dentist is too far or expensive	49 (3.4)	23 (3.4)	26 (3.4)	1.00 (0.56, 1.77)
Cost of dental care	41 (2.9)	15 (2.2)	26 (3.4)	1.55 (0.81, 2.95)
Not enough time to visit dentist	42 (2.9)	19 (2.8)	23 (3.0)	1.07 (0.58, 1.98)
A family member prevents dentist visit	36 (2.5)	14 (2.1)	22 (2.9)	1.40 (0.71, 2.76)
Nervous about visiting a dentist	37 (2.6)	20 (3.0)	17 (2.2)	0.74 (0.39, 1.43)
Source of dental health information~				
Family	1106 (77.6)	532 (79.6)	574 (75.8)	0.80 (0.62, 1.03)

School	653 (45.8)	312 (46.7)	341 (45.0)	0.94 (0.76, 1.15)
Dentist or dental hygienist	198 (13.9)	96 (14.4)	102 (13.5)	0.93 (0.69, 1.25)
Other health care worker	93 (6.5)	41 (6.1)	52 (6.9)	1.13 (0.74, 1.72)
Friend	460 (32.3)	206 (30.8)	254 (33.6)	1.13 (0.91, 1.42)
Community meeting	134 (9.4)	61 (9.1)	73 (9.6)	1.06 (0.74, 1.52)
Radio	763 (53.5)	369 (55.2)	394 (52.0)	0.88 (0.71, 1.08)
TV	217 (15.2)	115 (17.2)	102 (13.5)	0.75 (0.56, 1.00)

Data presented as No. (%) unless otherwise noted.
* Unadjusted odds ratio and 95% confidence interval
~ Multiple responses possible

Table 7: Dental health attitude of participants

Characteristic	All	Periodontal health	Periodontal disease	OR (95% CI)*
Reasons for teeth cleaning~				
Make teeth feel clean	1400 (98.2)	657 (98.4)	743 (98.2)	0.89 (0.40, 1.97)
Make teeth look clean	1390 (97.5)	651 (97.5)	739 (97.6)	1.07 (0.55, 2.10)
Prevent caries	1418 (99.5)	664 (99.4)	754 (99.6)	1.51 (0.34, 6.79)
Prevent bleeding gums	1412 (99.1)	660 (98.8)	752 (99.3)	1.82 (0.59, 5.60)
Prevent ulcers	1414 (99.2)	661 (99.0)	753 (99.5)	1.99 (0.58, 6.84)
Prevent foul breath	1412 (99.1)	660 (98.8)	752 (99.3)	1.82 (0.59, 5.60)
I was taught I should	571 (40.1)	275 (41.2)	296 (39.1)	0.92 (0.74, 1.13)
Things that prevent more teeth cleaning~				
Too much bother	451 (31.7)	196 (29.3)	255 (33.7)	1.23 (0.98, 1.53)
Not enough time	257 (18.0)	114 (17.1)	143 (18.9)	1.13 (0.86, 1.49)
Cost of toothbrush or paste	73 (5.1)	32 (4.8)	41 (5.4)	1.14 (0.71, 1.83)
No one else around me cleans their teeth	217 (15.2)	91 (13.6)	126 (16.7)	1.27 (0.95, 1.70)
Teeth or gums hurt when I clean teeth	64 (4.5)	25 (3.7)	39 (5.2)	1.40 (0.84, 2.34)
Teeth are not dirty	252 (17.7)	144 (21.6)	108 (14.3)	0.61 (0.46, 0.80)
Cleaning teeth doesn't help	114 (8.0)	70 (10.5)	44 (5.8)	0.53 (0.36, 0.78)
I was never taught to clean teeth	519 (36.4)	252 (37.8)	267 (35.3)	0.90 (0.72, 1.11)
I don't think it necessary	533 (37.4)	264 (39.6)	269 (35.5)	0.84 (0.68, 1.04)
I forget to clean teeth	148 (10.4)	75 (11.2)	73 (9.6)	0.84 (0.60, 1.18)

Data presented as No. (%) unless otherwise noted.
* Unadjusted odds ratio and 95% confidence interval
~ Multiple responses possible

Table 8: Association between participant characteristics and periodontal disease status

	Periodontal disease OR (95% CI)
Model 1 – Maternal characteristics (n=1,457)	
Age	**1.03 (1.00, 1.06)**
Gravidity	1.10 (0.89, 1.35)
Model 2 – Model 1 + Oral hygiene behaviors (n=1,425)	
Age	**1.03 (1.00, 1.06)**
Gravidity	1.06 (0.86, 1.32)
Toothbrush	0.86 (0.63, 1.17)
Datiwan	1.09 (0.83, 1.44)
Increased teeth cleaning during pregnancy	0.62 (0.36, 1.09)
Model 3 – Models 1-2 + Oral health knowledge & attitudes (n=1,424)	
Age	**1.03 (1.00, 1.06)**
Gravidity	1.07 (0.86, 1.33)
Toothbrush	0.89 (0.65, 1.21)
Datiwan	1.13 (0.86, 1.49)
Increased teeth cleaning during pregnancy	0.64 (0.36, 1.12)
Teeth and gums are not dirty	**0.70 (0.51, 0.96)**
Cleaning teeth and gums doesn't help	0.66 (0.42, 1.04)
Cleaning teeth is a bother	1.23 (0.98, 1.55)
Family a source of dental health information	0.83 (0.64, 1.08)
TV a source of dental health information	0.79 (0.58, 1.06)
Final model – Models 1-3 + Socioeconomic status (n=1,423)	
Age	**1.04 (1.01, 1.07)**
Gravidity	1.05 (0.84, 1.31)
Toothbrush	0.96 (0.70, 1.33)
Datiwan	1.07 (0.81, 1.42)
Increased teeth cleaning during pregnancy	0.63 (0.35, 1.12)

Teeth and gums are not dirty	**0.70 (0.51, 0.97)**
Cleaning teeth and gums doesn't help	0.67 (0.42, 1.06)
Cleaning teeth is a bother	1.26 (1.00, 1.59)
Family a source of dental health information	0.85 (0.66, 1.11)
TV a source of dental health information	0.83 (0.61, 1.13)
Electricity in the home	0.80 (0.52, 1.24)
House construction material	**0.78 (0.62, 0.99)**
Roof construction material	0.83 (0.53, 1.29)
Latrine in home	0.81 (0.63, 1.03)
Literacy	1.17 (0.76, 1.79)
Education	0.93 (0.70, 1.23)

Figure 1: Percent of sites bleeding on probing (BOP) among participants with gingivitis or periodontitis

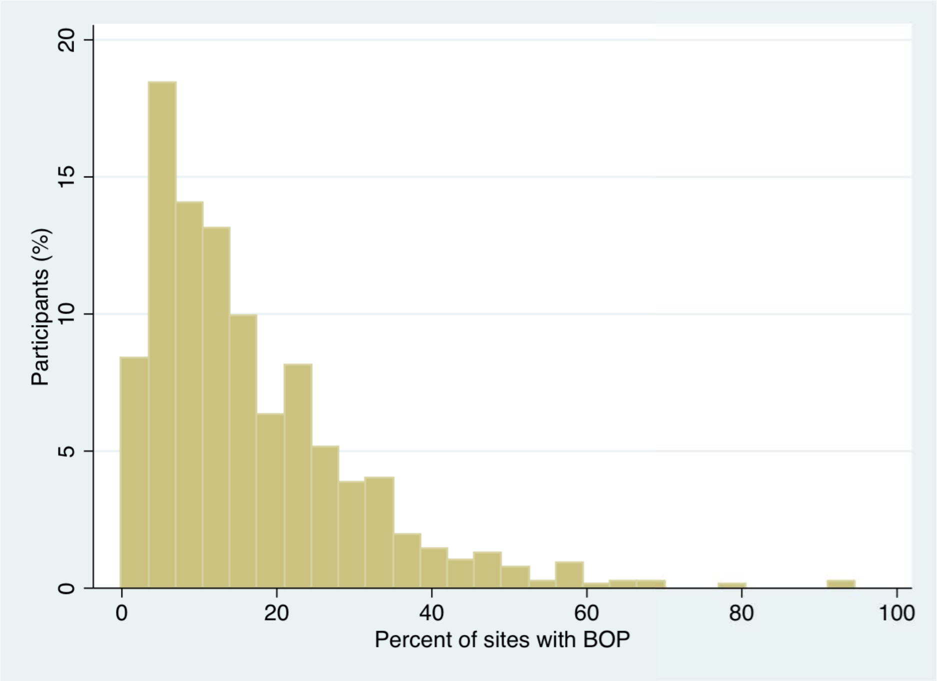
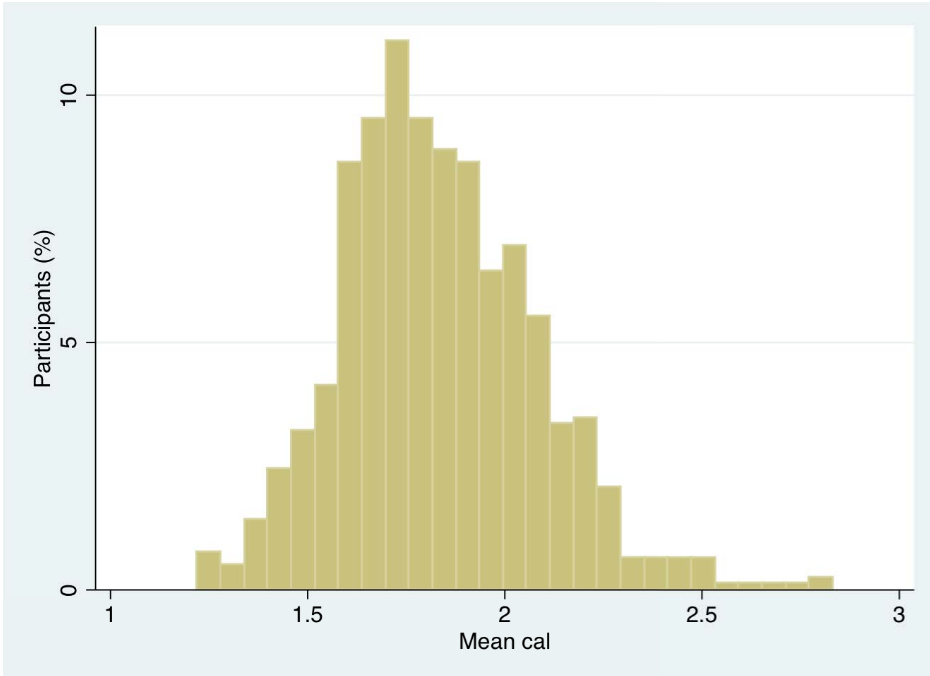


Figure 2: Mean clinical attachment loss (CAL) among participants with gingivitis or periodontitis



Chapter 5: Periodontal disease and preterm birth in rural Nepal: A community-based, prospective cohort study

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Background

Annually, almost 3 million babies die prior to 28 days of life, and preterm birth is the leading cause of these deaths in both high- and low-income settings.[1] Preterm babies that survive are at substantial risk of mortality from other causes, long-term disability, including neurological and developmental impairments, and non-communicable diseases.[2] In low- and middle-income countries (LMICs), where the majority of preterm babies are born, therapeutic interventions are often unavailable and difficult to scale up, especially in communities where many mothers deliver at home or in primary facilities without skilled care (e.g. South Asia).[3]

Periodontal disease includes a group of inflammatory conditions, typically initiated by oral bacteria, progressing from reversible accumulation of plaque and inflammation of gingival tissue (gingivitis) to irreversible breakdown of the supportive tissues of the teeth and eventually tooth loss (periodontitis).[4] Globally, gingivitis is highly prevalent, and severe periodontitis affects 10% to 15% of adult populations.[5] There is strong observational evidence for an association between periodontal disease in pregnant women and preterm birth,[6,7] but randomized controlled trials (RCTs) evaluating the impact of periodontal therapy during pregnancy on adverse pregnancy outcomes have produced inconsistent results.[8] Although the mechanisms underlying the observed association are unclear, hypotheses include hematogenic translocation of periodontal pathogens or their byproducts to the fetal-placental unit or the action of inflammatory mediators in the periodontium on levels of systemic inflammation.[9] Alternatively, the observed relationship could have arisen from a common confounding factor, such as a genetic hyper-inflammatory phenotype, responsible for both the increased risk for periodontal disease and adverse pregnancy outcomes.[10]

Investigations of the periodontal disease and preterm birth relationship have nearly universally been facility-based, whether in high- or low-income settings. Understanding this relationship from a population-based perspective in low resource communities is essential, and can offer certain benefits from an epidemiological and inferential perspective. Many populations in LMICs have lower prevalence of important confounding factors of this relationship, such as smoking, alcohol use, and chronic diseases (e.g. hypertension or diabetes). Community-based studies may avoid selection bias associated with hospital-based studies, particularly in populations where home delivery remains common, as is the case in South Asia. Given these potential benefits, we conducted a community-based, prospective cohort study to estimate the association between periodontal disease and preterm birth among women in a rural community in the Terai region of Nepal.

Methods

This community-based, prospective cohort study of periodontal disease and adverse pregnancy outcomes was conducted in a sub-area of Sarlahi District, Nepal between January and November 2016. We identified pregnant women <26 weeks gestation using the infrastructure of a large community-based randomized trial, the Nepal Oil Massage Study (NOMS) (NCT01177111), which was actively enrolling a population-based sample of pregnant women in this study area. Data collectors from this trial visited all women of childbearing age in this community at home every five weeks to identify new pregnancies.

Five auxiliary nurse-midwives were trained in basic dental anatomy, pathology, and the procedures for periodontal examination by an experienced dentist (NKA) from the Department of Dentistry, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. Training for these "community-based oral health workers" included identification of plaque and calculus, signs of gingivitis, and measurement of probing depth (PD), bleeding on probing (BOP), and distance from the cemento-enamel junction to the free gingival margin (CEJ-GM). Oral health workers were also trained in clinical research methods and ethics for human subjects research. Training lasted 3-4 weeks and included classroom instruction and practice of periodontal techniques under the guidance of the dentist. We estimated the validity of PD measurements taken by the oral health workers relative to the dentist, finding that percent agreement, weighted kappa scores, and intraclass correlation coefficients, with an allowance of PD ±1 mm, exceeded 99%, 0.7, and 0.9, respectively, indicating an acceptable level of agreement.[11]

All study visits were conducted in participant homes because of the wide dispersion of households across this rural community and the impracticality of bringing participants to a central location. Each participant underwent a full mouth examination by one of the oral health workers, and a trained assistant recorded data on paper forms. Data on participant demographics, vital signs and morbidities during pregnancy, oral hygiene practices, care-seeking, and knowledge, and other characteristics were collected through a series of questionnaires administered over subsequent visits during the course of pregnancy. Data collection teams were notified of the birth outcome by a locally resident study staff member, and the date of birth and other data concerning the mother and newborn were collected by the team as soon as possible after delivery. All data collection forms were electronically entered into a central database by experienced data entry operators.

Periodontal measurements were made using a color Williams probe (Hu-Friedy, Chicago, IL, USA). PD was measured on six sites per tooth (disto-, mid-, and mesial- aspects of buccal and lingual surfaces) and the CEJ-GM distance on two sites per tooth (mid- buccal and lingual aspects), excluding third molars. After probing each quadrant, the presence or absence of BOP was recorded for buccal and lingual surfaces of each tooth. PD values were recorded in millimeters from 1 to 10, rounded to the next higher whole number. CEJ-GM distances were recorded similarly, with values of 0 to 10 millimeters. If the free gingiva was coronal to the CEJ, the CEJ-GM measurement was recorded as 0. Clinical attachment loss (CAL) was calculated by summing PD and the CEJ-GM distance; the

CEJ-GM distance was assigned a value of 0 for distal and mesial sites, where this measure was not collected.

Clinical periodontal disease status was categorized into four definitions based upon our interest in the condition as an exposure with potential for systemic effects, particularly adverse pregnancy outcomes.[12] The primary definition classified periodontal health as all tooth sites PD <3 mm or PD 3 with no BOP and periodontal disease as ≥1 site PD 3 mm and BOP or PD ≥4 mm. Our secondary definition stratified participants into quartiles by the number of tooth sites either PD 3 mm and BOP or PD ≥4 mm. A third definition categorized participants by severity of gingivitis: 0 sites BOP, ≥1 site & <10% of sites BOP, ≥10% & <25% of sites BOP, and ≥25% of sites BOP. The fourth definition categorized participants according to periodontitis severity: 0 sites CAL ≥4 mm, ≥1 site CAL ≥4 mm, ≥1 site CAL ≥5 mm, and ≥1 site CAL ≥6 mm. Gestational age was calculated using last menstrual period (LMP) as recalled by the mother at the 5-weekly pregnancy surveillance home visits. Preterm birth was defined as a live birth at less than 37 weeks gestation.

This study was designed to have 80% power to detect relative risk of preterm birth >1.5, assuming a prevalence of preterm birth of 17% and periodontal disease of 15%, yielding a sample size of 1,475 pregnancies. Bivariate analyses between participant characteristics and the outcome, preterm birth, were evaluated using t-tests and logistic regression for continuous and binary/categorical variables, respectively. We calculated unadjusted and adjusted relative risks (RR & aRR) of preterm birth and associated 95% confidence internals (CI) using log-binomial regression. Several models were run to examine the effect of groups of covariates, including maternal characteristics, oral hygiene behaviors, and socioeconomic factors, on the relationship of interest for four definitions of periodontal disease. Covariates associated with preterm birth at the $p<0.10$ level in bivariate analyses were considered in the regression models. Additional variables, known through previous studies to be confounders of the periodontal disease and preterm birth relationship, were also included in regression, including age and gravidity. All statistical analyses were performed in STATA 14.2 (StataCorp, College Station, TX, USA).

This study received ethical approved from the Institutional Review Board at Johns Hopkins Bloomberg School of Public Health (Baltimore, USA) and the Ethical Review Board of the Nepal Health Research Council (Kathmandu, Nepal).

Results

Between January 11, 2016, and November 26, 2016, 1,900 pregnant women <26 weeks gestation were identified in the study area by the parent trial as eligible for enrollment in the cohort study (Figure 1). Of the eligible women, six declined to participate, 1,454 were enrolled, and the remainder were not visited due to logistical constraints for the purposes of cohort study. During the study follow-up period, 32 women were unreachable for administration of the questionnaire on oral hygiene behaviors and 265 were lost (mainly due to moving out to the study area; returning to maternal home for delivery is a traditional practice in this region) and did not provide a birth outcome.

Baseline demographic, periodontal, oral hygiene, and dental health care seeking characteristics of participants by periodontal disease status were previously reported.[13] At enrollment, mean gestation was 14.7 (SD: 4.4) weeks (range: 6.4 to 25.4 weeks). Age averaged 23.0 ± 4.6 years and was significantly higher among women with periodontal disease (mean difference: 1.28, 95% CI: 0.73, 1.82). Women with no previous pregnancies, relative to those with 1-3 pregnancies, were less likely to have periodontal disease (OR: 0.72, 95% CI: 0.55, 0.95), as were women with any education, relative to those with none (OR: 0.74, 95% CI: 0.58, 0.94), although these two associations were largely attributable to confounding by age. Women who lived in houses constructed of wood, brick, or stone (OR: 0.70, 95% CI: 0.55, 0.89); had electricity in their home (OR: 0.54, 95% CI: 0.34, 0.87); or had access to a latrine (OR: 0.72, 95% CI: 0.57, 0.92) were less likely to have periodontal disease, independent of age. Other characteristics, including literacy, BMI, and self-reported symptoms of urinary or vaginal infection, did not differ significantly across exposure groups. Several known confounders of the periodontal disease and preterm birth relationship had a reported prevalence near 0% in this study population, including smoking and other tobacco use, alcohol use, and hypertension. Between full term and preterm groups, only height (mean difference: -1.04 cm, 95% CI: -2.01, -0.08) and weight (mean difference: -1.82 kg, 95% CI: -3.03, -0.61) differed significantly at the <0.05 level (Table 1).

Less than half (46.3%) of participants had periodontal health according to our primary definition (Table 2). Of those with periodontal disease (53.7%), 44.3% had gingivitis and 9.4% periodontitis. Most participants (80%) had BOP, with more than a third (34.9%)

bleeding at ≥10% of sites and 11.3% at ≥25% of sites. Relatively few participants had any sites with CAL ≥4 mm (15.5%), ≥5 mm (4.7%), or ≥6 mm (1.6%). Nearly ten percent (9.3%) of participants had at least 1 site with PD 3 mm and bleeding or PD ≥4 mm, 19.9% had between 2-5 sites, and a quarter (24.7%) had >5 sites. One hundred and forty-five women (13.5%) delivered preterm, of which 128 (88.3%) were moderate preterm (<37 to ≥32 weeks), 15 (10.3%) very preterm (<32 to ≥28 weeks), and 2 (1.4%) extremely preterm (<28 weeks). Over three-quarters of participants (838 [77.7%]) were full term and 96 (8.9%) were postterm (>42 weeks). Mean gestation was 39.2 (SD: 2.4) weeks with a range of 26.6 and 49.1 weeks.

Unadjusted preterm birth rates were similar between women with periodontal health and disease for all four definitions of disease. In the final adjusted model for the primary definition of periodontal disease (≥1 site PD 3 mm and BOP or PD ≥4 mm), the relative risk of preterm birth for women with disease, compared to those without, was 1.21 (0.89, 1.66) (Table 3). In this model, time spent cleaning teeth (aRR: 1.01, 95% CI: 1.00, 1.03) and house construction material (aRR: 1.50, 95% CI: 1.09, 2.06) were significantly associated with preterm birth. The second disease definition stratified participants by number of disease sites, and the final adjusted model showed a significantly elevated risk of preterm birth (aRR: 1.46, 95% CI: 1.00, 2.11) for women with 2-5 diseased sites, relative to women with none (Table 4). In this model, maternal height was associated with lower risk of preterm birth (aRR: 0.97, 95% CI: 0.94, 1.00) and time spent cleaning teeth and house construction material were associated with higher risk of preterm birth of a magnitude similar to that seen in final model for the primary definition of periodontal disease. The unadjusted preterm birth rate was higher, although non-significantly, among participants with 1 diseased site (15.3%) or 2-5 diseased sites (17.2%) compared to those with 0 sites (12.4%). Risk for preterm birth did not vary significantly across levels of gingivitis (Table 5) or periodontitis (Table 6) severity in final adjusted models for either of these definitions.

Discussion

Our data demonstrate a slight association between periodontal disease, identified early in pregnancy, and preterm birth among women in a rural community in the Terai region of Nepal. We selected our primary definition of periodontal disease to reflect the hypothesized causal action of this exposure on systemic outcomes, such as preterm birth. Probing depth (PD) served as an estimate of the subgingival mucosal area accessible to microorganisms and bleeding on probing as an indicator of the presence of active inflammation.[12] We assessed the risk of preterm birth for participants by stratifying our primary exposure (≥1 site PD 3 mm and BOP or PD ≥4 mm) by the total number of "diseased sites" per participant. Relative to women with no diseased sites, there was a 46% increase in risk of preterm birth in women with 2-5 diseased sites and a non-significant increase of 31% in women with 1 diseased site. Secondary definitions for severity of gingivitis or periodontitis showed no association with preterm birth, although associations between periodontitis and preterm should be interpreted cautiously as the number of women with the condition was low.

Observational studies have provided strong evidence for an association between periodontal disease and preterm birth. A meta-analysis by Chambrone et al. (2011) found a pooled relative risk of 1.70 (1.03, 2.81) between periodontitis and preterm birth, although there are important differences between previous studies of this relationship and our study population.[14] Age, an important confounder of this association, was lower in our study population (23.0 ± 4.6) than observed elsewhere; a review of twenty-five community-based studies of periodontal disease and adverse pregnancy outcomes in low- and middle-income countries (LMICs) found average ages (for studies reporting the measure) ranging from 26 to 29.[15] Prevalence of important risk factors, such as smoking and chronic diseases, were higher among participants in other studies, especially those based in high-income countries.[14] The young age and low levels of these risk factors, despite the absence of preventative dental services, likely contributed to the low prevalence of mild periodontitis and near absence of severe periodontitis observed in our population, relative to previous studies. A stronger association between periodontal disease and preterm birth may have been seen in our population had there been higher prevalence and greater severity of periodontitis, as would be expected in an older population.

A number of large randomized controlled trials (RCTs) intervening on mothers with periodontal therapy during pregnancy have failed to see a reduction in the incidence of preterm birth.[7,16-21] Theories have been proposed relating to the effectiveness of periodontal therapy – typically a non-surgical procedure to remove plaque and calculus called root scaling and planing, which is delivered early in pregnancy – in fully disrupting the exposure-outcome pathway between periodontal disease and preterm birth.[22] Lopez et al. (2015) point out that several RCTs reporting the failure of periodontal therapy to prevent preterm birth were not successful in eliminating periodontal infection in the intervention group, a prerequisite to affecting the supposed causal pathway.[23] Lopez et al. (2015) showed that a subset of RCTs, which were high in quality and able to demonstrate elimination of periodontal disease in the intervention group, found reductions in preterm birth.[23] Similarly, another meta-analysis by Kim et al. (2012) identified a subset of RCTs, those with populations at high risk of preterm birth, for which periodontal therapy successfully reduced preterm birth.[24] Xiong el al. (2011) have considered the optimal timing of periodontal treatment during pregnancy, suggesting that the mechanical manipulation of the gingiva involved may inadvertently trigger bacteremia, contributing increased risk of adverse pregnancy outcomes in some cases, thus attenuating observation of any true effect of the therapy in intervention trials.[25] To eliminate this risk, Xiong et al. (2011) suggest that periodontal therapy be delivered to women prior to pregnancy, an approach particularly suited to low- and middle-income countries (LMICs), where there is little access to preventative care and non-surgical procedures could be conducted by dental hygienists after appropriate training.[11,25] Offenbacher et al. (2009) hypothesize that success in averting the influence of periodontal disease as an exposure may be dependent upon the ability of interventions to more effectively control the microbiome of the oral cavity, in addition to restoring periodontal health according to traditional clinical measures.[20]

Most of these previous trials have treated women with moderate to severe periodontitis with the aim of reducing preterm birth, but few have targeted women with mild periodontitis or gingivitis.[14,26] Gingivitis is prevalent among adults and pregnancy is associated with aggravation of existing the disease.[27] Over 80% of participants in our study population had gingivitis and very few signs of periodontitis, a burden of disease profile likely attributable to the young age and poor oral hygiene habits of these pregnant women. A meta-analysis by George et al. (2011), found that periodontal treatment was more effective in reducing preterm birth among women with less severe periodontal disease (defined as PD <4 mm).[28] A trial by Lopez et al. (2005) included 870 women with gingivitis in hospital setting in Santiago, Chile, finding a significantly higher risk of preterm low birth weight among those not treated for gingivitis (aOR: 2.76, 95% CI: 1.29, 5.88).[1]

Gingivitis requires less intensive treatment than periodontitis, and can include good oral hygiene, use of an antiseptic oral rinse, and periodontal therapy. Antiseptic oral rinses are well known for their ability to reduce plaque and control inflammation, however, their action on pregnancy outcomes is underexplored.[29,30] A meta-analysis by Boutin et al. (2013) reported that trials using chlorhexidine oral rinse as a co-intervention in the treatment group resulted in statistically significant reductions in preterm birth.[8] Jeffcoat et al. (2011) were able to achieve a reduction in incidence of preterm birth in a high-risk population with the use of chlorhexidine oral rinse intervention.[31] Another study, by Jiang et al. (2016), provided women with a cetylpyridinium chloride oral rinse and oral hygiene education, finding improved periodontal health but no change in the rate of preterm birth,

[1] Adjusted odds ratio and corresponding 95% confidence interval (aOR, 95% CI)

although they did observe a reduction in risk for premature rupture of membranes.[32] Additional studies of women with pregnancy-associated gingivitis should further explore the potential to reduce risk of adverse pregnancy outcomes through oral health care interventions, especially antiseptic oral rinses and oral hygiene education.

A strength of this study was that it was conducted in a low-income country and a community-based setting. Unlike the majority of studies of periodontal disease and preterm birth conducted in high-income countries, the prevalence of several important confounders of this relationship, e.g. smoking, alcohol use, and chronic diseases, were very low in our study population. Nearly all studies of this relationship, at any income level, have been conducted in hospital-based settings, introducing the risk of selection bias. A review by our research team found that only one study recruited participants using a population-based sample in an LMIC.[15] This study, carried out by Mobeen et al (2008) in a periurban area of Hyderabad, Pakistan, found associations of varying degrees between measures of periodontal disease and neonatal deaths, perinatal deaths, and stillbirth.[33] Community-based trials in LMICs are needed to evaluate the effectiveness of oral health interventions in populations at high risk of adverse pregnancy outcomes.

A limitation of this study was the collection of clinical recession measures from only the direct buccal and lingual surfaces, a decision taken to limit the study visit time. In the absence of these data, we likely underestimated the burden of periodontal disease among pregnant women in this study, potentially attenuating our measure of association. We were also unable, due to logistical constraints, to control for some important confounders of this relationship, including previous preterm birth, chronic disease (e.g. diabetes), and used only a proxy (self-reported symptoms) for urinary tract and vaginal infections. Lastly, preterm birth was based upon maternal self-report of last menstrual period (LMP) instead of the best obstetric estimate, including ultrasound examination.[34] To limit error associated with maternal recall, data collectors visited women in this study every five weeks to identify new pregnancies.

Conclusion

This study found a slight association between periodontal disease and preterm birth among pregnant women <26 weeks gestation in a sub-area of Sarlahi District, Nepal. Few studies of this relationship have been conducted in rural community settings in low-income countries. Women in these populations have a burden of periodontal disease and confounding risk factors that differs from what has been observed in high-income countries. Future studies should evaluate the effectiveness of community-based oral health interventions on the incidence of preterm birth and other adverse pregnancy outcomes in low-income countries with high risk for these outcomes.

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Table 1: Characteristics of participants in the cohort study

Characteristic	**All**	**Term**	**Preterm**	**Mean difference / OR (95% CI)***
Age				
Year (mean ± SD)	23.0 ± 4.6	23.1 ± 4.6	22.8 ± 4.8	-0.31 (-1.12, 0.49)
Age (years)				
<18	116 (10.8)	97 (10.4)	19 (13.1)	1.31 (0.77, 2.22)
18-<35	945 (87.6)	822 (88.0)	123 (84.8)	Ref
≥35	18 (1.7)	15 (1.6)	3 (2.1)	1.34 (0.38, 4.68)
Ethnic group				
Hills (Pahadi)	85 (7.9)	76 (8.1)	9 (6.2)	Ref
Plains (Madeshi)	994 (92.1)	858 (91.9)	136 (93.8)	1.34 (0.66, 2.73)
Height				
Cm (mean ± SD)	150.8 ± 5.5	150.9 ± 5.6	149.9 ± 5.3	**-1.04 (-2.01, -0.08)**
Weight				
Kg (mean ± SD)	45.8 ± 6.9	46.1 ± 7.0	44.3 ± 5.9	**-1.82 (-3.03, -0.61)**
BMI				
Underweight	309 (28.6)	260 (27.8)	49 (33.8)	1.27 (0.87, 1.85)
Normal weight	711 (65.9)	619 (66.3)	92 (63.4)	Ref
Overweight or obese	59 (5.5)	55 (5.9)	4 (2.8)	0.49 (0.17, 1.38)
High blood pressure				
No	1071 (99.3)	927 (99.3)	144 (99.3)	Ref
Yes	8 (0.7)	7 (0.7)	1 (0.7)	0.92 (0.11, 7.53)
Gravidity		0		
First pregnancy	307 (28.5)	261 (27.9)	46 (31.7)	1.21 (0.82, 1.79)
1-3 previous pregnancies	645 (59.8)	563 (60.3)	82 (56.6)	Ref
≥4 pregnancies	127 (11.8)	110 (11.8)	17 (11.7)	1.06 (0.61, 1.86)
Urinary or vaginal infection~				
No	831 (77.0)	724 (77.5)	107 (73.8)	Ref
Yes	248 (23.0)	210 (22.5)	38 (26.2)	1.22 (0.82, 1.83)
Literacy				

No	574 (53.2)	500 (53.5)	74 (51.0)	Ref
Yes	505 (46.8)	434 (46.5)	71 (49.0)	1.11 (0.78, 1.57)
Education (years)				
0	576 (53.4)	498 (53.3)	78 (53.8)	Ref
1-9	296 (27.4)	262 (28.1)	34 (23.4)	0.83 (0.54, 1.27)
≥10	207 (19.2)	174 (18.6)	33 (22.8)	1.21 (0.78, 1.88)
Electricity				
No	85 (7.9)	76 (8.1)	9 (6.2)	Ref
Yes	994 (92.1)	858 (91.9)	136 (93.8)	1.34 (0.66, 2.73)
House construction material				
None, thatch, sticks, or bamboo	658 (61.0)	579 (62.0)	79 (54.5)	Ref
Wood planks, bricks, or stone	421 (39.0)	355 (38.0)	66 (45.5)	1.36 (0.96, 1.94)
House roof material				
None, plastic, thatch, or grass	83 (7.7)	69 (7.4)	14 (9.7)	Ref
Tile/tin/concrete	996 (92.3)	865 (92.6)	131 (90.3)	0.75 (0.41, 1.36)
Latrine				
No latrine	478 (44.3)	413 (44.2)	65 (44.8)	Ref
Brick, concrete, or pit latrine	601 (55.7)	521 (55.8)	80 (55.2)	0.98 (0.69, 1.39)

Data presented as No. (%) unless otherwise noted

* T-test or unadjusted odds ratio and 95% confidence interval as appropriate

~ Self reported symptoms of painful urination or foul smelling vaginal discharge during the course of pregnancy

Table 2: Periodontal disease status of participants

Characteristic	All	Term	Preterm	Rate of preterm
1. Periodontal health, gingivitis, or periodontitis				
Health (All sites PD <3 mm or PD=3 mm & no BOP)	500 (46.3)	438 (46.9)	62 (42.8)	12.4%
Gingivitis/Periodontitis	579 (53.7)	496 (53.1)	83 (57.2)	14.3%
- Gingivitis (≥1 site PD 3 mm & BOP, but no sites PD ≥4 mm)	478 (44.3)	407 (43.6)	71 (49.0)	14.9%
- Periodontitis (≥1 site PD ≥4 mm)	101 (9.4)	89 (9.5)	12 (8.3)	11.9%
2. Number of "diseased" sites (PD 3 mm & BOP or PD ≥4 mm)*				
0 sites	500 (46.3)	438 (46.9)	62 (42.8)	12.4%
1 site	98 (9.1)	83 (8.9)	15 (10.3)	15.3%
2-5 sites	215 (19.9)	178 (19.1)	37 (25.5)	17.2%
>5 sites	266 (24.7)	235 (25.2)	31 (21.4)	11.7%
3. Gingivitis severity				
0 sites BOP	212 (19.7)	185 (19.8)	27 (18.6)	12.7%
≥1 site & <10% of sites BOP	490 (45.4)	422 (45.2)	68 (46.9)	13.9%
≥10% & <25% of sites BOP	255 (23.6)	211 (23.7)	34 (23.5)	13.3%
≥25% of sites BOP	122 (11.3)	106 (11.4)	16 (11.0)	13.1%
4. Periodontitis severity				
0 sites CAL ≥4	912 (84.5)	786 (84.2)	126 (86.9)	13.8%
≥1 site CAL 4 & no sites ≥5	116 (10.8)	105 (11.2)	11 (7.6)	9.5%
≥1 site CAL 5 & no sites ≥6	34 (3.2)	28 (3.0)	6 (4.1)	17.6%
≥1 site CAL ≥6	17 (1.6)	15 (1.6)	2 (1.4)	11.8%

Data presented as No. (%) unless otherwise noted

* Levels of this variable were determined by stratifying the number of diseased sites into quartiles

Table 3: Association between periodontal disease and preterm birth

Characteristic	**Model 0 (n=1,801)**	**Model 1 (n=1,081)**	**Model 2 (n=1,060)**	**Final model (n=1,060)**
Periodontal disease (gingivitis or periodontitis)	1.16 (0.85, 1.58)	1.18 (0.87, 1.61)	1.16 (0.85, 1.59)	1.21 (0.89, 1.66)
Age		1.00 (0.96, 1.04)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)
Height (cm)		0.99 (0.96, 1.02)	0.99 (0.96, 1.02)	0.99 (0.96, 1.02)
Weight (kg)		**0.97 (0.94, 1.00)**	0.97 (0.94, 1.00)	0.97 (0.94, 1.00)
Primiparous		1.22 (0.85, 1.76)	1.24 (0.86, 1.79)	1.24 (0.86, 1.79)
Time spent cleaning teeth (mins)			1.01 (1.00, 1.02)	**1.01 (1.00, 1.03)**
Times per day teeth cleaned			1.25 (0.69, 2.28)	1.31 (0.72, 2.37)
Cleans teeth in the evening			0.57 (0.29, 1.10)	0.53 (0.27, 1.02)
Toothbrush use			1.50 (0.98, 2.30)	1.44 (0.94, 2.22)
Datiwan use			1.26 (0.88, 1.81)	1.32 (0.92, 1.88)
Finger use			0.68 (0.25, 1.31)	0.70 (0.36, 1.34)
Danta manjhan use			0.71 (0.44, 1.15)	0.71 (0.44, 1.15)
House construction material				**1.50 (1.09, 2.06)**

Table 4: Association between number of diseased sites and preterm birth

Characteristic	**Model 0 (n=1,081)**	**Model 1 (n=1,081)**	**Model 2 (n=1,060)**	**Final model (n=1,060)**
Periodontal health (0 diseased sites)	Ref	Ref	Ref	Ref
Periodontal disease (1 diseased site)	1.24 (0.74, 2.09)	1.36 (0.81, 2.28)	1.28 (0.76, 2.14)	1.31 (0.78, 2.20)
Periodontal disease (2-5 diseased sites)	1.39 (0.96, 2.03)	1.39 (0.95, 2.02)	1.40 (0.97, 2.04)	**1.46 (1.00, 2.11)**
Periodontal disease (>5 diseased sites)	0.94 (0.63, 1.41)	0.94 (0.63, 1.42)	0.92 (0.61, 1.39)	0.96 (0.64, 1.46)
Age		1.01 (0.97, 1.05)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)
Height (cm)		0.99 (0.96, 1.02)	0.99 (0.96, 1.02)	0.99 (0.96, 1.02)
Weight (kg)		**0.97 (0.94, 0.99)**	0.97 (0.94, 1.00)	**0.97 (0.94, 1.00)**
Primiparous		1.23 (0.85, 1.78)	1.25 (0.87, 1.80)	1.25 (0.87, 1.80)
Time spent cleaning teeth (mins)			1.01 (1.00, 1.02)	**1.01 (1.00, 1.03)**
Times per day teeth cleaned			1.26 (0.69, 2.29)	1.31 (0.72, 2.39)
Cleans teeth in the evening			0.57 (0.29, 1.11)	0.53 (0.27, 1.03)
Toothbrush use			1.53 (0.99, 2.35)	1.47 (0.96, 2.27)
Datiwan use			1.29 (0.90, 1.84)	1.34 (0.94, 1.92)
Finger use			0.69 (0.36, 1.33)	0.71 (0.37, 1.36)
Danta manjhan use			0.70 (0.43, 1.13)	0.70 (0.43, 1.13)
House construction material				**1.49 (1.09, 2.05)**

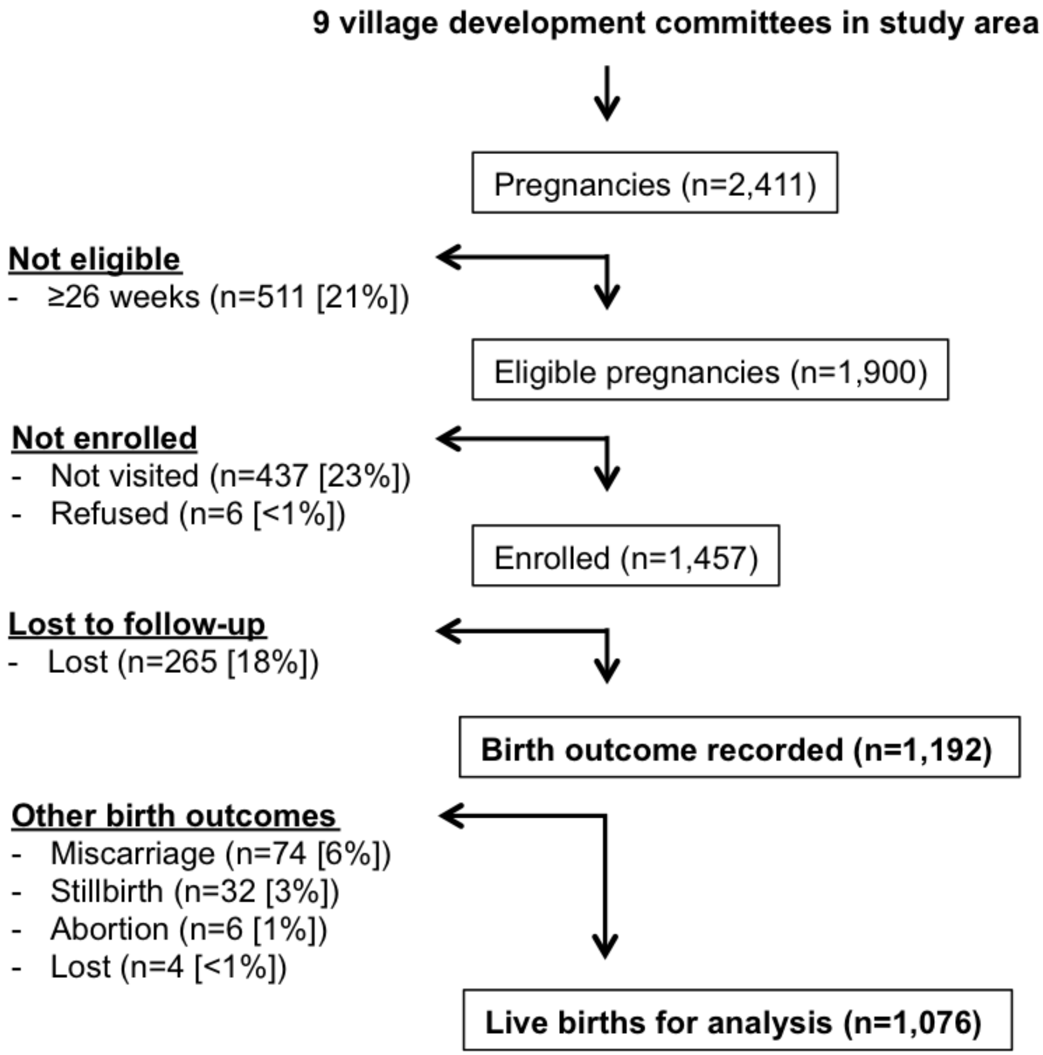
Table 5: Association between gingivitis severity and preterm birth

Characteristic	Model 0 (n=1,081)	Model 1 (n=1,081)	Model 2 (n=1,060)	Final model (n=1,060)
No gingivitis	Ref	Ref	Ref	Ref
Gingivitis (≥1 site & <10% of sites)	1.10 (0.73, 1.67)	1.13 (0.74, 1.70)	1.20 (0.79, 1.82)	1.20 (0.79, 1.81)
Gingivitis (≥10% & <25% of sites)	1.06 (0.66, 1.69)	1.05 (0.66, 1.69)	1.09 (0.68, 1.76)	1.11 (0.69, 1.79)
Gingivitis (≥25% of sites)	1.04 (0.58, 1.85)	1.02 (0.57, 1.82)	1.02 (0.56, 1.84)	1.03 (0.57, 1.87)
Age		1.00 (0.97, 1.05)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)
Height (cm)		0.99 (0.96, 1.02)	0.99 (0.96, 1.02)	0.99 (0.96, 1.02)
Weight (kg)		**0.97 (0.94, 1.00)**	0.97 (0.94, 1.00)	0.97 (0.94, 1.00)
Primiparous		1.22 (0.85, 1.76)	1.24 (0.86, 1.79)	1.24 (0.86, 1.79)
Time spent cleaning teeth (mins)			1.01 (1.00, 1.02)	1.01 (1.00, 1.03)
Times per day teeth cleaned			1.24 (0.68, 2.25)	1.29 (0.71, 2.33)
Cleans teeth in the evening			0.57 (0.30, 1.11)	0.54 (0.28, 1.04)
Toothbrush use			1.49 (0.97, 2.29)	1.43 (0.93, 2.19)
Datiwan use			1.28 (0.89, 1.83)	1.33 (0.93, 1.89)
Finger use			0.67 (0.35, 1.29)	0.69 (0.36, 1.33)
Danta manjhan use			0.71 (0.44, 1.15)	0.71 (0.44, 1.14)
House construction material				**1.46 (1.07, 2.01)**

Table 6: Association between periodontitis severity and preterm birth

Characteristic	Model 0 (n=1,081)	Model 1 (n=1,081)	Model 2 (n=1,060)	Final model (n=1,060)
Periodontitis (0 sites with CAL ≥4)	Ref	Ref	Ref	Ref
Periodontitis (≥1 site with CAL ≥4)	0.69 (0.38, 1.23)	0.70 (0.39, 1.27)	0.73 (0.41, 1.32)	0.75 (0.42, 1.34)
Periodontitis (≥1 site with CAL ≥5)	1.28 (0.61, 2.69)	1.21 (0.57, 2.56)	1.14 (0.54, 2.40)	1.16 (0.55, 2.43)
Periodontitis (≥1 site with CAL ≥6)	0.85 (0.23, 3.17)	0.77 (0.21, 2.87)	0.97 (0.27, 3.57)	1.02 (0.28, 3.75)
Age		1.01 (0.97, 1.05)	1.00 (0.96, 1.04)	1.00 (0.96, 1.04)
Height (cm)		0.99 (0.96, 1.02)	0.99 (0.96, 1.03)	0.99 (0.96, 1.02)
Weight (kg)		**0.97 (0.94, 1.00)**	0.97 (0.94, 1.00)	**0.97 (0.94, 1.00)**
Primiparous		1.21 (0.84, 1.75)	1.23 (0.85, 1.78)	1.23 (0.86, 1.78)
Time spent cleaning teeth (mins)			1.01 (1.00, 1.02)	1.01 (1.00, 1.03)
Times per day teeth cleaned			1.24 (0.68, 2.25)	1.29 (0.71, 2.34)
Cleans teeth in the evening			0.58 (0.30, 1.11)	0.54 (0.28, 1.04)
Toothbrush use			1.50 (0.97, 2.30)	1.44 (0.94, 2.21)
Datiwan use			1.27 (0.89, 1.82)	1.32 (0.92, 1.89)
Finger use			0.68 (0.35, 1.31)	0.70 (0.36, 1.35)
Danta manjhan use			0.71 (0.44, 1.16)	0.71 (0.44, 1.15)
House construction material				**1.46 (1.07, 2.01)**

Figure 1: Cohort study participation flow chart



Chapter 6: Discussion

Summary of key findings

We reviewed the literature on community-based observational and interventional studies of the periodontal disease and adverse pregnancy outcome association in low- and middle-income countries (LMICs). Community-based studies were defined as studies recruiting patients: 1) in a home setting using a population-based sample, 2) in two or more hospitals or antenatal clinics, or 3) in a single institution responsible for a portion of the population's deliveries that was sufficiently large to presume broad representativeness. We identified only one study that recruited participants in a home setting using a population-based sample. This study by Mobeen et al. (2008) found significant associations of varying degrees between measures of periodontal disease and neonatal deaths, perinatal deaths, and stillbirth among women in a periurban setting in Pakistan. Two trials, five cohort studies, and 17 case-control or cross-sectional studies enrolled participants in multiple institutions in a single community. Studies were widely heterogeneous in population and methodology, and their results were mixed.

We evaluated the ability of community-based oral health workers with 3-4 weeks training to accurately conduct a periodontal examination in a rural home setting that is common in Nepal. Percent agreement, weighted kappa scores, and intraclass correlation coefficients, with an allowance of ±1 mm, exceeded 99%, 0.7, and 0.9, respectively, demonstrating an acceptable level of agreement with an experienced dentist. Lower agreement was observed on posterior teeth, lingual surfaces, and proximal sites, which are areas that may be more difficult to measure accurately and have been associated with lower agreement in previous studies. Our results suggest that shifting tasks like periodontal examination from highly trained periodontal examiners to community-based oral health workers could be utilized for data collection in future studies or as a potential strategy to increase access to dental health services.

Roughly half of women in the study population had signs of gingivitis or periodontitis according to our primary periodontal disease definition. The majority of women had some sites that bled on probing, but every few had substantial pocketing or gingival recession. Our population had important differences with populations in similar studies, including a younger age distribution, lower prevalence of important risk factors for periodontal disease and preterm birth, and limited access to dental health care. We found older age and living in a house constructed with less sturdy materials to be associated with periodontal disease. Participants tended to clean their teeth only once per day, typically in the morning, and few had ever visited a dentist or other dental health professional. More than a quarter of participants reported not using a toothbrush and almost half used datiwan, a twig fashioned from a variety of local trees, for teeth cleaning. Almost no participants used interdental cleaning methods or antiseptic oral rinse.

The primary aim of this research project was to assess the relationship between periodontal disease and preterm birth among women early in pregnancy in the Terai region of Nepal. We found a small but statistically significant increase in the risk of preterm birth (<37 weeks gestation) in women with mild periodontal disease relative to those with periodontal health. Our primary definition of periodontal disease was selected to reflect the hypothesized causal link between infection and inflammation in the periodontium and adverse pregnancy outcomes. This definition classified women by the number of diseased sites (≥1 site PD 3 mm and BOP or PD ≥4 mm) identified during periodontal examination. More time spent cleaning teeth and living in a house constructed with sturdy materials were also positively associated with preterm birth. No associations with preterm birth were observed for our secondary exposure definitions that stratified participants by gingivitis or periodontitis severity.

Limitations

The main limitations of the descriptive and main association analyses in the cohort study concern data collection for the exposure, confounding, and outcome variables. Gingival recession was not measured on distal and mesial sites due to time constraints, potentially yielding an underestimate of the burden of periodontal disease in our study population. Some relevant clinical periodontal measures, such as gingival or plaque indices, were not collected for the same reason. These data would have provided a more complete picture of the oral health status of participants. Some potential confounders of the periodontal disease and preterm birth relationship, including previous preterm birth and chronic diseases (e.g. diabetes), were not assessed. Data on two important confounders, urinary tract or vaginal infections, were collected using only self-reported symptoms, which are poor proxies for more sensitive diagnostic tests, and may have resulted in residual confounding. Gestational age for the study outcome, preterm birth, was calculated using maternal recall of last menstrual period (LMP) alone, in place of the best obstetric estimate, which includes the use of ultrasonography. Consequently, there may have been some unnecessary measurement error in the outcome associated with imperfect recall and variability in length of the menstrual cycle or timing of ovulation.

Our validation sub-study, which evaluated the accuracy of periodontal examinations conducted by community-based oral health workers, included two major limitations. First, the study only evaluated the validity of examiners' measurements relative to the senior dentist, ignoring inter-reliability among the oral health workers or intra-reliability between repeated examinations by individual oral health workers. Second, low levels of periodontal disease observed in this study population limited our ability to evaluate the validity measurements on sites with deep pockets and substantial recession. Sites with these conditions have been shown in previous studies to be associated with higher measurement error. Utilizing a larger sample size, older population, or clinic-based population with higher prevalence and severity of periodontal disease may have helped to address these limitations.

The primary limitation of our literature review was the inability to conduct a pooled analysis of the results due to heterogeneity in study design, methodology, and quality among previous studies. Our definition of a "community-based study," which was used to classify studies for inclusion in the review, was relatively non-specific because of variations in the data on study populations, especially important confounders, provided by each study. Lastly, categorizing studies by high-, middle-, and low-income groups ignored variation between sub-populations within countries, and may have led us to exclude studies from high-income countries that were relevant or overlook differences in populations within included studies.

Recommendations for future research

Our study reported a small but statistically significant association between periodontal disease early in pregnancy and risk of preterm birth among women in the Terai region of Nepal. There may be benefit to evaluating the effect of oral health interventions on pregnancy outcomes in similar rural, low-income communities, especially given that few preventative interventions for preterm birth exist. One approach would be to assess the effect of a package of oral health interventions, including oral hygiene education and antiseptic oral rinse, on the incidence of preterm birth in a community with high risk of the condition. In areas similar to Sarlahi District, Nepal, where rates of neonatal mortality and preterm birth are high, oral health interventions, if able to reduce the incidence of preterm birth even slightly, could result in substantial public health impact.

Before an intervention trial would be undertaken, however, there are a number of additional analyses that could be conducted using data collected by our study that might help clarify the relationship between periodontal disease and adverse pregnancy outcomes in this population. First, we plan to examine the associations between periodontal disease and several other adverse pregnancy outcomes, including low birth weight, small-for-gestational age (SGA), and pre-eclampsia. Our team will also explore relationships between subgingival biofilm composition and gingival and serum inflammation between full term and preterm women, using gingival crevicular fluid

(GCF), plaque, blood serum specimens that were collected from each participant during the course of this cohort study.

Additional information will also be provided by a subset of 175 women in the cohort study that participated in a small pilot trial of three anti-septic oral rinses: cetylpyridinium chloride (0.05%), chlorhexidine (0.12%), and salt and water. Using data from this trial, we will measure the adherence and acceptability of participants to the three oral rinses, as well as estimate the change in biofilm composition, inflammatory markers, and periodontal measurements after 12 weeks of oral rinse use, comparing women in each rinse group to a control group. This analysis will determine the feasibility of administering an oral rinse intervention in a rural community and assess the effectiveness of the rinse in reducing the burden of aggressive periodontal bacteria, markers of gingival or serum inflammation, and the prevalence of periodontal pocketing and bleeding on probing in women in this trial.

Lastly, a different, but overlapping, subset of women in the cohort study received an ultrasound examination (<22 weeks gestation) conducted by community-based health workers. We will compare these ultrasound examinations to estimates of gestational age derived from maternal recall of last menstrual period (LMP) at the participant home visits, which were made every 5 weeks as part of the parent trial's pregnancy surveillance. If possible, we will incorporate the ultrasound-based estimates of gestational age into our calculation of preterm birth, which could help to reduce measurement error, increase the specificity of our outcome, and generate improved estimates of the association between periodontal disease and preterm birth. Future research could explicitly aim to assess the validity and reliability of ultrasound-based gestational age estimates collected by community-based health workers relative to highly trained physicians or technicians.

Further studies might also explore the ability of community-based oral health workers to provide oral health treatment, such as root scaling and planing, at home in rural communities. With proper training and oversight, utilizing community-based oral health workers to conduct periodontal examinations and/or provide periodontal therapy could greatly increase access to dental health care in low-income settings. Whether for the purpose of research or practical health service delivery, future efforts should assess the intra- and inter-rater reliability of periodontal examinations conducted by community-based oral health workers.

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Curriculum Vitae

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PERSONAL INFORMATION

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EDUCATION

Expected 2017	**Doctor of Philosophy (PhD)** Global Disease Epidemiology and Control Department of International Health Johns Hopkins Bloomberg School of Public Health Baltimore, MD, USA Advisor: Dr. Luke Mullany Thesis project: *Periodontal disease and preterm birth in rural Nepal: A community-based, prospective cohort study*
May 2012	**Master of Public Health (MPH)** Health Systems and Policy Concentration Johns Hopkins Bloomberg School of Public Health Baltimore, MD, USA Advisor: Dr. Orin Levine Capstone project: *Global Immunization Coverage and Conflict*
May 2012	**Certificate** in Vaccine Science and Policy Johns Hopkins Bloomberg School of Public Health Baltimore, MD, USA
May 2007	**Bachelor of Arts (BA)** in Biology Rice University Houston, TX, USA

RESEARCH EXPERIENCE

Mar 2015–Jun 2017	**Graduate Student Researcher**, Department of International Health, Johns Hopkins Bloomberg School of Public Health. Led a

community-based, prospective cohort study to assess the incidence of preterm birth among women with and without periodontitis in rural Nepal. Conducted a pilot trial to evaluate adherence to and acceptability of several antiseptic oral rinses among pregnant women.

Mar 2015–May 2015 **Consultant**, United States Agency for International Development. Performed statistical analyses to evaluate relationships between neonatal death, health service utilization, and newborn care practices using data from a neonatal verbal autopsy study in six districts across Nepal. Made program recommendations for Nepal's Community-based Newborn Care Package.

Sep 2011–Mar 2015 **Communications Assistant (from Sep 2011) | Research Associate (from Nov 2012) | Graduate Student Researcher (from Sep 2013)** International Vaccine Access Center, Department of International Health, Johns Hopkins Bloomberg School of Public Health. Conducted a qualitative study to describe the barriers to accountability in the routine immunization system in Niger State, Nigeria. Analyzed data from a national survey of immunization managers about accountability issues in Nigeria's health system. Provided technical support for communications around country introductions of pneumococcal conjugate vaccine and global pneumonia control efforts.

PROFESSIONAL EXPERIENCE

Jul 2017–Present **Director**, Global Health Strategies, New Delhi, India

Jun 2013–Jun 2015 **Secretary, Board of Directors**, Disability Rights Maryland, Baltimore, MD

Jun 2013–Jan 2017 **Member, Board of Directors**, Disability Rights Maryland, Baltimore, MD

Oct 2010–May 2011 **Project Manager**, Department of Special Education, University of Makeni, Makeni, Sierra Leone

June 2010–May 2011 **Consultant**, Various consultancies in public health, development, and communications, Freetown, Sierra Leone

May 2009–May 2010 **Volunteer**, Prosthetics Outreach Foundation, Prosthetic and Orthotic Clinic, Makeni, Sierra Leone

Jul 2007–May 2009	**Program Associate**, Rice 360° Institute for Global Health Technologies, Rice University

TEACHING EXPERIENCE

Spring 2014	**Teaching Assistant**, Global Disease Control Programs & Policy Department of International Health Johns Hopkins Bloomberg School of Public Health
Fall 2014	**Teaching Assistant**, Introduction to International Health Department of International Health Johns Hopkins Bloomberg School of Public Health
Fall 2014	**Teaching Assistant**, Vaccine Development and Application Department of International Health Johns Hopkins Bloomberg School of Public Health
Fall 2013	**Teaching Assistant**, Global Disease Control Programs & Policy Department of International Health Johns Hopkins Bloomberg School of Public Health
Spring 2008 & 2009	**Teaching Assistant**, Cain Project in Engineering and Professional Communication, Intercultural Engineering Communication, Rice University

PEER REVIEWED PUBLICATIONS

2017	**Erchick D**, George A, Umeh C, Wonodi C. Understanding internal accountability in Nigeria's routine immunization system: Perspectives from officials at the national, state, and local levels. Int J Health Policy Manag. 2017; 6(7):403-412.
2016	George A, **Erchick D**, Mahmud M, Yau I, Wonodi C. Sparking, supporting, and steering change: Grounding an accountability framework with viewpoints from Nigerian routine immunization and primary health care government officials. Health Policy Plan. 2016; 31(9):1326-32.

ABSTRACTS & PRESENTATIONS

Mar 2014	Constela D, **Erchick D**, Wonodi C. Evaluating the cost-effectiveness of vaccine against pneumococcal disease in Nigeria. Abstract accepted for poster presentation at 9th International

	Symposium on Pneumococci and Pneumococcal Diseases. Hyderabad, India
May 2012	**Erchick D**. Global Immunization Coverage and Conflict. Oral presentation at MPH Capstone Symposium. Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
Mar 2010	**Erchick D**. Prosthetic Technologies for Developing Countries. Oral presentation, 2nd Annual Health & Biomedical Symposium. Freetown, Sierra Leone
Jul 2008	**Erchick D**, Richards-Kortum R. Bioengineering and Global Health. Oral presentation at the Knowledge is Power Program (KIPP) Foundation School Summit. San Antonio, TX
Apr 2008	**Erchick D**, Driskill L. Service Learning Instruction. Oral presentation at the Conference on College Composition and Communication. New Orleans, LA

HONORS AND AWARDS

2017	**Nancy Stephens Award** Johns Hopkins Bloomberg School of Public Health
2016	**Procter & Gamble Fellowship** Johns Hopkins Bloomberg School of Public Health
2016	**Baker, Reinke, Taylor Scholarship in International Health** Johns Hopkins Bloomberg School of Public Health
2015	**Global Health Field Research Award** Johns Hopkins Bloomberg School of Public Health
2014	**Clements-Mann Fellowship in Vaccine Sciences** Johns Hopkins Bloomberg School of Public Health
2010	**Linda Faye Williams Social Justice Prize** Rice University
2009	**Wagoner Foreign Study Scholarship** Rice University